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Hemodynamic Optimization: The Latest Strategies for Fluid and Blood Management

Location: Rooms Brussels & Oslo – CCIB Barcelona

Date and Time: Monday September 29th, 12:30 to 14:00
Lunch will be provided

Chairperson: Michael R. Pinsky

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The Evolving Role of Hemodynamic Monitoring in the ICU

Michael R. Pinsky, MD, CM, Dr hc, FCCP, FCCM

Professor of Critical Care Medicine, Bioengineering, Anesthesiology, Cardiovascular Diseases, and Clinical & Translational Sciences
Vice Chair for Academic Affairs UPMC, Pittsburgh, Pennsylvania, USA

How to Best Guide Fluid Management:
Role of Noninvasive Assessment of Fluid Responsiveness

Azriel Perel, MD

Professor and Chairman Department of Anaesthesiology and Intensive Care
Sheba Medical Center, Tel Aviv University, Tel Hashomer, Israel

Patient Blood Management and Transfusion Optimization

Keith J Ruskin, MD

Professor of Anesthesiology and Neurosurgery
Yale University School of Medicine, New Haven, Connecticut, USA

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- Care of the Multiple Organ Donor
- Prevention of Perioperative Complications
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- Adequate Dialysis in the ICU
- Role of Intensivists in Emergency Mass Critical Care
- Interview with Daniel de Backer
- Country Focus: Chile

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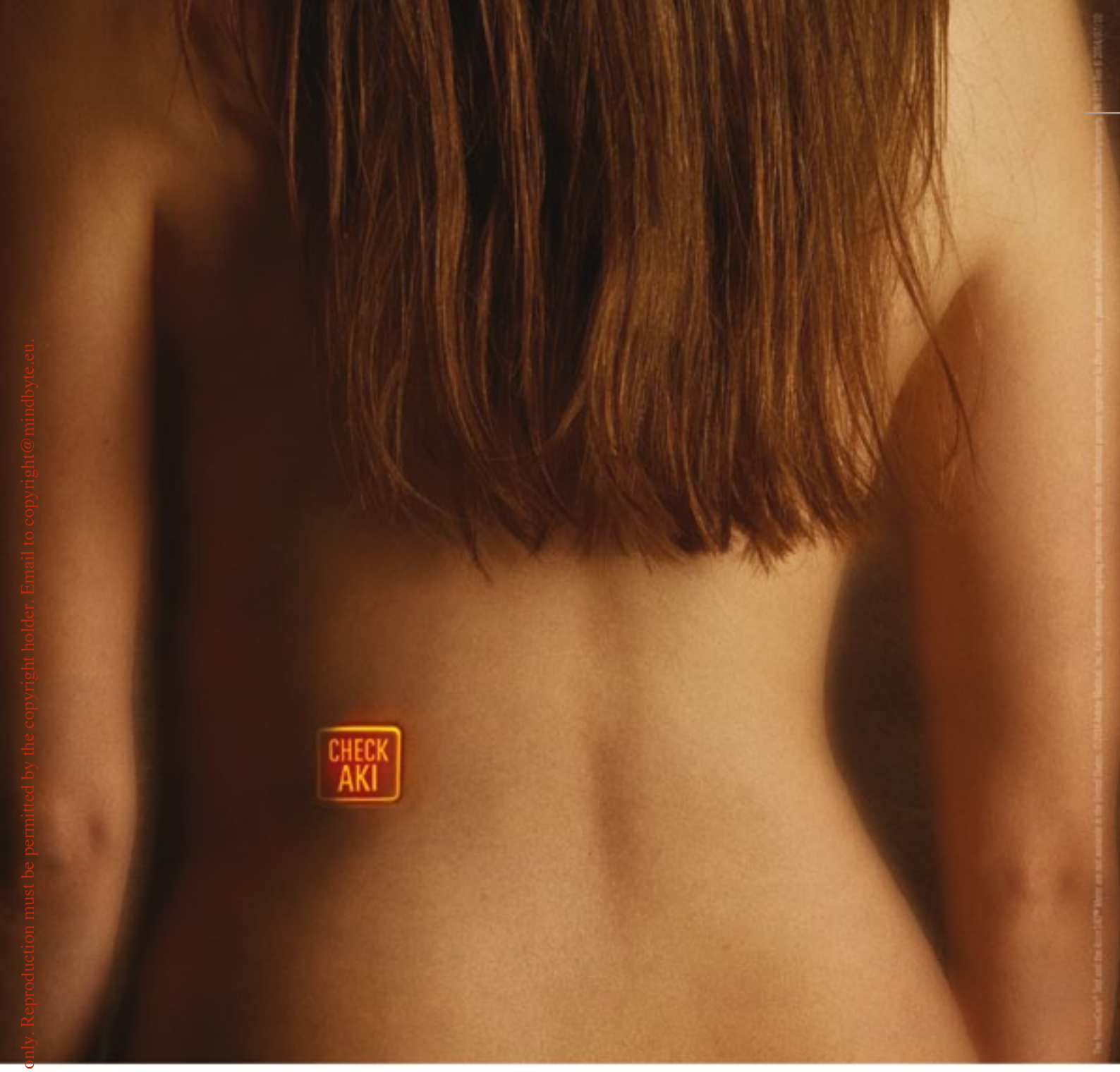

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COMMUNICATION

Jean-Louis Vincent

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Communication skills are perhaps even more important in intensive care medicine than in other specialties. Critical illness can be frightening for both patients and families, and it is a given that errors in communication can impede care and even harm the patient. But when time and resources are stretched, what is the best way to communicate? In the first article in our cover story, Taylor Thompson and Lillian Ananian write about family presence on ICU work rounds. Recognising that poor communication probably underlies many of the conflicts that develop between ICU clinicians and families, they trialled inviting families on ICU work rounds. They outline the benefits their medical ICU has experienced and consider the potential downsides. They conclude that it is an opportunity to exchange information, build trust and make the ICU workplace more enjoyable. Next, Paul Barach and Gautham Suresh look at how to improve handoffs – the crucial process that ultimately ensures that the patient's care continues without errors. Handoff is often affected by communication barriers, and Barach and Suresh look at the scale and causes of the problem, how handoffs can be studied and improved, potential solutions and training.

Continuing our series on Fluids, Manu Malbrain, Johan Huygh and Joost Wauters discuss the different parameters related to bio-electrical impedance analysis and their use to monitor fluid status and guide fluid management.

Our Matrix starts with Jaume Mestre and Néstor Bacelor's article on care of the multiple organ donor. They outline best practice in caring for the donor, with the aim of reversing the derangements resulting from previous disease and brain death, stabilising the donor and helping to obtain more and better functioning organs. Next, Yuda Sutherasan, Raquel Rodríguez-González and Paolo Pelosi consider prevention of perioperative complications, inspired by the saying "It takes a village to raise a child." Collaboration is needed to improve outcomes, they argue. Michael Reade follows with a review of bleeding, coagulopathy and blood products in major trauma. With evidence for existing practice being challenged, there are implications for blood supply, and new therapies are being investigated. He writes that regulators must balance caution with innovation in what has, until recently, been an evidence-free field. Lastly, Zaccaria Ricci, Gianluca Villa, Stefano Romagnoli and Claudio Ronco discuss the multidimensional aspects of adequate dialysis in the ICU. They detail basic concepts related to the dialytic dose, current evidence available on the topic, and explain the concept of adequacy.

The role of intensivists in emergency mass critical care (EMCC) is explored by Mary King and Niranjan Kissoon in the Management section. They advocate better education about EMCC so that ICU providers may be better prepared and organised during future disasters. They argue that intensivists also have a professional obligation to play an integral role along the continuum of EMCC planning and delivery.

Daniel De Backer is President-Elect of the European Society of Intensive Care Medicine (ESICM). He is our interview subject this issue, and talks about his aspirations for ESICM as well as his thoughts on priorities for intensive care research.

Our Country Focus visits Chile. Intensive care medicine is a relatively young discipline in that country. Sebastián Ugarte explains in his glance at intensive care medicine that while economic development has led to more investment in healthcare, the challenge is to qualify enough intensivists to keep up with demand. Ugarte joins Juan Espinoza to write about the use of ECMO. Following disappointing results in the H1N1 pandemic of 2009, results since then have been promising with the development of ECMO referral centres and availability of well-trained personnel.

The European Society of Intensive Care Medicine meets in Barcelona in September. Please drop by the ICU Management booth 26. We are always delighted to meet our readers and contributors. Hope to see you there!

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

Jean-Louis Vincent

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ICU Management

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Sniffing Out C. Difficile

Rapid detection of C. difficile could be on its way with the development by UK scientists of an 'electronic nose.'

Using a mass spectrometer, the researchers have shown that it is possible to identify the unique 'smell' of C-diff, which would lead to rapid diagnosis.

In addition, the scientists say it could be possible to identify different strains of the disease simply from their smell – a chemical fingerprint.

The team have measured the Volatile Organic Compounds (VOCs) given out by different of strains of Clostridium difficile, and have shown that many of them have a unique 'smell'. In particular, different strains show different chemical fingerprints, which are detected by a mass spectrometer.

University of Leicester chemists developed the 'electronic nose' for sniffing volatiles and collaborated with a colleague in microbiology who has a large collection of well characterised strains of Clostridium difficile.The work suggests that the detection of the chemical fingerprint may allow for a rapid means of identifying C. difficile infection, as well as providing markers for the way the different strains grow.

Professor Paul Monks, from the Department of Chemistry, said: "The rapid detection and identification of the bug Clostridium difficile (often known as C-diff) is a primary concern in healthcare facilities. Rapid and accurate diagnoses are important to reduce Clostridum difficile infections, as well as to provide the right treatment to infected patients.

"Delayed treatment and inappropriate antibiotics not only cause high morbidity and mortality, but also add costs to the healthcare system through lost bed days. Different strains of C. difficile can cause different symptoms and may need to be treated differently so a test that could determine not only an infection, but what type of infection could lead to new treatment options."

Professor Monks added: "Our approach may lead to a rapid clinical diagnostic test based on the VOCs released from faecal samples of patients infected with C. difficile. We do not underestimate the challenges in sampling and attributing C. difficile VOCs from faecal samples."

Dr Martha Clokie, from the Department of Microbiology and Immunology, added: "Current tests for C. difficile don't generally give strain information - this test could allow doctors to see what strain was causing the illness and allow doctors to tailor their treatment."

Professor Andy Ellis, from the Department of Chemistry, said: "This work shows great promise. The different strains of C-diff have significantly different chemical fingerprints and with further research we would hope to be able to develop a reliable and almost instantaneous tool for detecting a specific strain, even if present in very small quantities."

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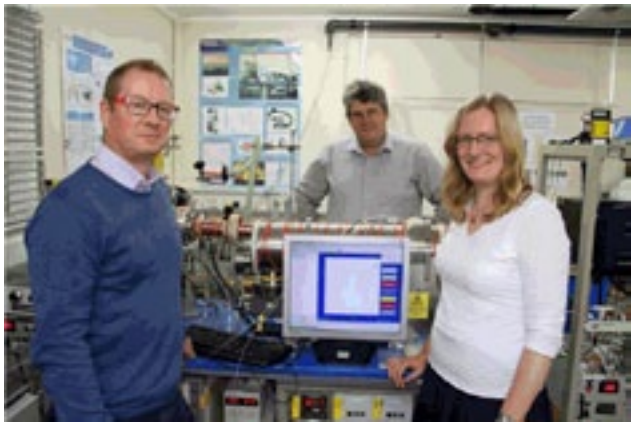

L-R Professor Andy Ellis, Professor Paul Monks and Dr Martha Clokie from the University of Leicester. Credit: University of Leicester

Life After Sepsis

A survey about the problems that sepsis survivors face starts on World Sepsis Day, 13 September. Open for participation for 1 year, the survey will be available initially in English, French and German, with additional languages to follow. For more information, visit the World Sepsis Day website http://www.world-sepsis-day.org

Experts Gather to Discuss Glucose Control in the Critically Ill

On Monday, September 29, 2014, global experts will convene for a symposium to discuss the practicalities and economic implications of implementing glucose control for critically ill patients. Held from 12:30-14:00, and supported by Edwards Lifesciences, the symposium forms part of the 27th annual conference of the European Society of Intensive Care Medicine (ESICM), held in Barcelona, Spain.

Titled "Further advancements in making improved glucose control a reality," the event will be chaired by Valentin Fuhrmann (Hamburg, Germany) and Michael Hiesmayr (Vienna, Austria). Speakers include Jean-Charles Preiser (Brussels, Belgium), Hazra Moeniralam (Nieuwegein, The Netherlands) and James Krinsley (Stamford, USA).

Linked as an independent predictor of mortality, dysglycemia is a common, serious, and potentially costly healthcare problem in critically ill patients.[1] Studies have suggested a potential benefit to customizing target glycemic levels based on patient diagnosis, diabetic status and pre-admission diabetic management.[2,3,4,5] New tools, including continuous glucose monitoring, can provide the data needed to raise standards of care.

Join us for this lunch symposium or visit www.edwards.com/eu/cgm to register.

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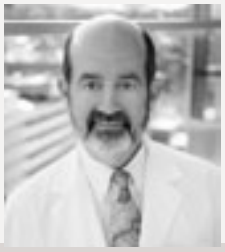
FAMILY PRESENCE ON ICU WORK ROUNDS



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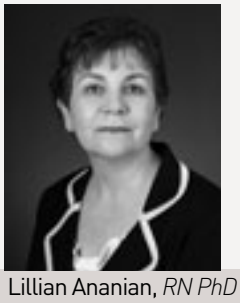

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Good communication is essential for optimal patient and family outcomes and to align treatments with the patient's goals and preferences. Unfortunately, substantial evidence suggests that ICU clinicians are not meeting family expectations for good or even adequate communication during an ICU stay. Two studies indicate that a third to nearly half of families fail to comprehend the diagnosis, prognosis or ICU treatments (Azoulay et al. 2001; 2002). Studies of families' perceptions indicate that poor communication may lead to anxiety and depression, and families desire more time with nurses and physicians (Pochard et al. 2005). Communication deficits may lead to mistrust, especially if the information provided is contradictory (Lautrette et al. 2007). In a recent survey of families of ICU survivors, 25 percent reported at least one episode where contradictory information was provided (Hwang et al. 2014).

Poor communication probably underlies many of the conflicts that develop between ICU clinicians and families. Conflicts contribute to stress and professional burnout and perceived conflicts are relatively common (Embriaco et al. 2007; Azoulay et al. 2009). One recent study reported that families or clinicians perceived conflict in the care of nearly two-thirds of ICU patients (Schuster et al. 2014). Curiously, when a clinician perceived that any conflict had developed between the ICU team and the family, the family shared this perception only half the time. Families' perceptions of conflicts were missed a third of the time by clinicians, and the physician/surrogate agreement on the presence of conflict was poor (kappa=0.14). Clearly we need much better communication strategies for the benefit of all concerned (Long and Curtis 2013).

> **"Poor communication probably underlies many of the conflicts that develop between ICU clinicians and families"**

Investigators have tested a number of interventions to improve communication and comprehension of families of ICU patients. A systematic review identified 21 publications of 16 distinct randomised controlled interventions (Scheunemann et al. 2011). These included printed information, structured family conferences, additional family support measures, and ethics and palliative care rounds or interventions. On balance, evidence suggests that these interventions improve comprehension, reduce family stress, and decrease the length and intensity of ICU treatments.

Recently, investigators have proposed videos and interactive computerised decision support tools to meet varying and complex family information needs in the ICU, and preliminary results with videos are promising (McCannon et al. 2012; Cox et al. 2014). A randomised trial of diaries completed by ICU clinicians summarising, in lay terms, the events of the day (including pictures), reduced symptoms of post-traumatic distress in ICU survivors, probably by filling in key information gaps after recovery (Jones et al. 2010). A pilot study of this intervention suggested this approach also may help the psychological recovery of families, perhaps by the same mechanism (Jones et al. 2012). However, substantial deficits in communication persist in many of the superior arms of these trials, suggesting more work is needed to improve communication.

ICU work rounds offer the opportunity to further involve families. Following an Institute of Medicine report endorsing "patient-centred care", the Committee on Hospital Care, American Academy of Pediatrics and the Institute for Family-Centered Care issued a joint policy statement encouraging rounds at the bedside (2003; 2012). Furthermore, these organisations suggest that family presence on rounds should be part of standard practice to improve communication. Clinical practice guidelines for family and patient-centered care of both adults and children have also been published (Davidson et al. 2007).

Two groups have evaluated family presence on work rounds in paediatric ICUs by surveying family perceptions (Aronson et al. 2009; Stickney et al. 2014). Both showed a high degree of family satisfaction (95-98%) and comfort with most aspects of being included on work rounds. In one PICU where all parents were invited to attend but not all parents chose to do so, demographic or socioeconomic variables did not predict who chose to attend work rounds (Stickney et al. 2014). Feeling welcome was the only characteristic that predicted parent's attendance (OR 12.2, 95% CI 2.3-64.8; p=.007). Attendees were more likely to agree that families should be invited than non-attendees (96% vs 81%). Most parents reported that they understood the content of rounds (84%), yet clinicians thought only 21% of parents understood ($p < 0.001$). This finding strongly suggests that ICU clinicians need to recalibrate their views on the value parents derive from participating in work rounds.

Both studies noted that physicians thought that teaching was reduced or less comfortable when parents were present, and both studies indicated a higher acceptance of family presence by nurses than physicians. Parents indicated some concerns about privacy, and in one survey 93% asked that the provider return for further discussions (Stickney et al. 2014).

The published experience in adult ICUs is limited. One trauma ICU noted that families reported having limited

clinical knowledge about their family member before attending work rounds. After being included in work rounds families reported that they obtained vital information, which allowed them to better understand the condition and plan of care (Schiller and Anderson, 2003). Investigators in a medical ICU evaluated the impact of inviting families to multidisciplinary rounds (Jacobowski et al. 2010). A higher degree of satisfaction was reported for frequency of communication and decisional support, though overall satisfaction was unchanged and some families felt rushed to make decisions. If attending ICU rounds educates families as ICU diaries appear to do, then psychological outcomes may also be improved (Jones et al. 2012). Of note, family presence during cardiopulmonary resuscitation (CPR) appears to ease the grieving process and reduces post-traumatic avoidance behaviour (Critchell and Marik, 2007).

Our medical ICU participated in a demonstration project funded by the Robert Wood Johnson Foundation to integrate palliative care expertise into our critical care practice (Billings et al. 2006). Open visitation was one of the many interventions that resulted. With families often present at the bedside during morning rounds it made little sense to ask them to leave (or close the door) and exclude them from our discussions. We followed the lead of our paediatric colleagues and began inviting families to our twice daily ICU work rounds. Our current practice is to clarify with the surrogate decision maker who among the family members present are authorised to hear protected medical information. We extend an invitation and assure families that participation is voluntary. For those accepting our invitation we introduce ourselves and give our roles on the team. We invite interruptions for any errors family members hear or perceive during the presentation of the history. Finally, we apologise in advance for the jargon they will be hearing and reassure families that they will have private time with us later during our usual family meetings.

Our subjective impressions are that nearly all families choose to attend rounds when invited and appear to benefit from the experience. It is not uncommon that we receive important corrections or clarifications to the patient's history. Some families say they found the experience engaging, and most were thankful for the time and effort the ICU team spent on their family member's behalf. Others remarked on the team's comprehensive approach to clinical problem-solving. Mindful that teaching has been reported to suffer from family presence, we make every effort to try and keep teaching on work rounds at a high level. Medical resident acceptance appears to be high. Our perception is that the time spent on work rounds has not increased substantially with family presence. Rather, overall rounding time appears to be less as family meetings later in the day are shorter and focused on clarifying information already presented or discussed. Further, nurses report that families appear to have a better understanding of current clinical issues such that it is much easier for nursing to help families process this information as they return to the bedside.

What are the downsides to family presence? As noted previously, physicians appear to be less enthusiastic about family presence than families or nurses and perceive less teaching (Stickney et al. 2014). The burdens this reticence places on learning and workplace stress is unknown. When the practice of allowing families to attend CPR first surfaced years ago, concerns were expressed that increased malpractice suits would result. These fears have not been realised (Davidson et al. 2007). While the impact of family presence in adult ICU rounds on malpractice rates is unknown, experts suggest that strengthening staff and family bonds actually decrease the likelihood of legal action (Brown 1989).

In summary, increased emphasis on family-centred care and persistent evidence of inadequate and inconsistent communication during the ICU stay strongly support new and improved efforts to improve family comprehension, understanding, and comfort. Growing awareness of the burden that conflicts exact on critical care providers and families further emphasise the need for better communication. Paediatric intensivists have involved parents in work rounds for many years and nearly all parents find rounds understandable and helpful. Nascent experiences in adult ICUs suggest this may also be true, but solid evidence is lacking. While it is too early to know if this practice in adult ICUs will help solve our communication gaps, rounding without families appears to us to be a lost opportunity to exchange information, build trust, and make the ICU workplace more enjoyable. ■

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ASSESSING AND IMPROVING COMMUNICATION AND PATIENT HANDOFFS IN THE ICU

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Introduction

The process of transferring responsibility for care of a patient from one healthcare provider or healthcare team to another is referred to as the "handoff," or "handover," while the term "signout" refers to the act of transmitting information about the patient (Berwick 1996). Patient handoffs occur several times a day between nurses, between attending physicians / nurse practitioners, and between trainees, when the patient is admitted to, managed in, and transferred from the intensive care unit. Clinicians and researchers agree that patient handoffs serve as the basis for transferring responsibility and accountability for the care of patients from outgoing to incoming healthcare teams across shifts, across disciplines and across care settings. During a handoff necessary and critical information about a patient is transmitted from one caregiver to the next, or from one team of caregivers to another. Information allows the health professionals or healthcare team that takes over the patient's care to gain relevant knowledge about the patient, understand the management plan, and ultimately ensure that the patient's care continues in an uninterrupted, error-free manner. The patient handoff between healthcare providers is a vulnerable period in the patient's care journey during which vital information may be lost, distorted or misinterpreted (Baker et al. 2005). Unfortunately, the practice of patient handoff to, within and from the ICU is often suboptimal due to communication barriers and is a major contributor to medical errors and adverse events.

How Frequent and Important is the Problem?

Studies find significant variation in practice and a lack of appreciation of the systems of care around the patient. Patient transfers from intensive care units (ICU) to other inpatient wards may be particularly vulnerable in this regard, given the unstable patient status and complexity of the medical conditions that characterise these transfers. A novel contribution to the literature on transitions of patient care is a deeper understanding of how variations in communication, culture, and technology used by healthcare professionals in medicine and nursing leads to ineffective or suboptimal handoffs. Studies of hospital discharge suggest a particularly risky care transition, especially for older adults. Multiple studies document that adverse events occur in approximately one in five adult medical patients within three weeks of discharge (Clark 1996). Nearly 20 percent of older Medicare patients discharged from a hospital will be readmitted within 30 days (Cohen et al. 2012). A broad spectrum of adverse events can occur after discharge, including both diagnostic and therapeutic errors, but adverse drug events (ADEs) are particularly common and harmful. Studies indicate that nearly 100,000 elderly patients are hospitalised every year due to ADEs (Cullen et al. 1997). Additionally, 1 in 67 emergency hospitalisations are the result of an ADE. Particularly in the face of an ageing population, ensuring safe care transitions for patients with complex, chronic illnesses remains an important patient safety issue (DeRienzo et al. 2014).

Patients are transferred from the ICU, where medical care is intensive and resources are rich, to environments where patients receive much less intensive monitoring and patient care. Often some key pieces of information are omitted, transmitted with errors, or not understood as intended (Eccles and Mittman 2006). When a patient's transition from the intensive care unit (ICU) to and from a hospital ward is less than optimal, the repercussions can be far-reaching — unit readmission, an adverse medical event, avoidable morbidity and even mortality (Flink et al. 2012). Similar evidence of implications of ineffective handoffs in the ICU setting can be seen in work by Li et al., who found that of 112 patient transfers poor communication during patient transfer resulted in 13 medical errors and two patients being transiently "lost" to medical care (Forster et al. 2003). A total of 101 NICU patient handoffs (31 unique patients) were analysed. DeRienzo et al. demonstrated that, per patient, residents made more written errors for infants in critical care beds than for infants in step-down beds (2.33 vs 1.67, p=0.04). Replacing residents' written handoffs with the gold standard, auto-populated data would have prevented 92% of written errors. Furthermore, in a survey about how providers perceived their handoffs strategies and practices, 60% of provider felt that handoffs were incomplete or missing key information.

What Are Some Causes of Poor Handoffs?

Discontinuity of care and lack of seamless transitions between the ICU and other hospital settings were present with poor handoffs in most studies, although the specific causes and contributing factors varied. In some cases local differences in the organisation and management of patient care played an important role. A fundamental reason, however, is the lack of a common ground to enable interpretation of the complete handoff content (Greenhalgh and Russell 2010). Common ground refers to the pertinent mutual knowledge, beliefs and assumptions that support interdependent action, and an ongoing process of tailoring, updating and repairing mutual understanding. It is constructed by three skills: the ability to

share, inform and request; the ability to jointly share attention and intentions with each other; and the ability to construct common cultural knowledge.(Toccafondi et al. 2012). According to Cohen and colleagues, true handoffs involve a co-construction by both parties of the oncoming caregiver's understanding of the patient, and not a one-way transmission of information (Hesselink et al. 2012a).

Poor information storage and retrieval systems that are not user-friendly also contribute to compromised handoffs (Hesselink et al. 2012b). For example, even with sophisticated electronic medical records, many ICUs continue to use paper forms or parallel electronic databases as repositories of patient information to transmit to incoming colleagues (Horwitz et al. 2009).

Other studies demonstrate that distractions during complex patient management tasks and lack of adequate time to complete documentation without interruptions contribute to key information being overlooked or not transferred (Hoskote et al. 2014). Asynchronous communication practices in which the patient's status and management plan are written down or audio-recorded by the outgoing professional and the information is ready or played back by the incoming team later to gain information about the patient can also contribute to errors and omission of key data (Jencks et al. 2009).

"Improving the management and effectiveness of ICU handoffs requires a clear plan, clinical championship, and … carefully laid out interventions"

How Can Patient Handoffs Be Studied And Improved?

Qualitative, quantitative and mixed improvement methods are needed to assess the impact of handoff interventions in the ICU. Such data are needed to explain results of rigorous evaluations, and to understand the relationships between contextual and contributory factors, as well as the sustainability, maintenance, scale-up and spread of interventions to improve handoffs. Implementation science and improvement science are maturing fields that encourage application of rigorous methods to study ICU quality problems, their root causes, the settings and contexts in which they occur, and the effects of strategies attempting to improve the quality of ICU care and ultimately improve patient outcomes (Johnson et al. 2012). Such improvement strategies require multi-level, multi-component, context-sensitive approaches, with continuous monitoring, evaluation and serial refinement of ICU practices.

In particular, qualitative research generates large amounts of data, and it is important that the purpose of the study drives the analysis (Johnson and Barach 2009; Kaplan et al. 2012). Ensuring reliability of the data is essential. "Scientifically rigorous" research has favoured multicentre studies, particularly those with rigorous experimental designs that control for context, quantitative data, and adherence to methodologies that reduce bias and confounding (Klein et al. 2005). This kind of research thus focuses on relationships among variables, to the exclusion of contextual features such as the attributes of the unique clinical settings and participants in the ICU in which interventions are studied, and the attributes of those where these interventions may be subsequently adopted or adapted. In contrast to this approach, some have proposed a "realist review" for the study of complex social and clinical interventions, noting that that traditional experimental designs may not be useful for, or adaptable to, evaluating interventions in complex, naturalistic settings, where resistance to uptake, and different expectations for the success of the project by multiple clinical groups can greatly undermine success and sustainability of interventions (Kripalani et al. 2007).

Some Solutions To Improving ICU Handoff Management (see Box 2, p10)

Improving handoffs in the ICU is a good system to measure the quality of handoffs. After initially developing local (ICU-specific) operational criteria for what constitutes an optimal handoff, the percentage of handoff sessions and individual patient handoffs that satisfy these criteria is a good place to start assessing effective signouts (see below). The unit of analysis will be (a) Each patient on whom patient hand-off is performed; and (b) Each handoff session during which information about one or more patients is transferred. The data can be gathered by one of the following methods:

- Self-report by the person providing the handoff;
- Self-report immediately after handoff by the person receiving the handoff;
- Self-report by the person receiving the handoff at the end of the shift;
- Assessment by a third party of direct observation of the handoff;
- Review of videorecording or audio recording of the handoff.

Once a pragmatic measurement system is developed, developing a single improvement approach for all handoffs is not possible because of the diversity and complexity of ICU settings, practices, management and resources. Ensuring quality and safety during times of transition will therefore require an approach that draws on all available wisdom about what is needed to improve handovers, coupled with a social-technical systems approach to understanding and improving care at the point where patients and providers meet (Kushner 2002). Improving the management and effectiveness of ICU handoffs requires a clear plan, clinical championship, and a series of carefully laid out interventions at several levels.

These interventions meet the definition of a "complex intervention," one in which it is difficult to isolate one or a small number of "active ingredients," and to standardise the setting in which the intervention is applied (Li et al. 2012). In an article about the complexity of evaluation of electronic health programmes, Greenhalgh and Russell comment on the limits of scientific evaluation, when it is applied to complex projects that have multiple components and multiple official and unofficial aims (Greenhalgh and Russell 2012). This is in contrast to the scientific method with an "interpretivist" approach that explicitly considers the importance of the perceptions and mindsets of participant clinicians relative to other aspects of the programme. Complex interventions to improve ICU care also call for new methods of evaluation of the economic and social benefits associated with their implementation and sustainability (McCormack et al. 2009).

Recognising the barriers to changing clinical practices around improving patient handoffs requires appreciating the heterogeneity and complexity of interventions implicit in improvement science, including rapid-cycle improvement methods, such as Plan-Do-Study-Act (PDSA) cycles that involve iterative cycles of planning, design, evaluation and refinement of improvement strategies (Medical Research Council 2008). These approaches generate evidence regarding barriers to improvement and help identify solutions and assess their effectiveness using quick turnaround in time and resources. An improvement-science approach recognises the need for customised, site-specific and context-sensitive solutions based on careful study of current practices and local mental models and careful surfac-

ing and recognition of barriers to improvement (Mohr et al. 2004). Context is recognised as important for the success and uptake of clinical interventions and helps to address difficulty of reaching all staff for handoff training, staff resistance to use of structured signout, and concerns that structured handoff may initially increase the time taken to complete signout (Patterson and Wears 2010; Pawson and Tilley 1997).

Training For Improved Patient Handoffs

Effective ICU handoffs should be comprehensive, accurate, unambiguous and efficient. Verbal sign-out should be augmented with written materials. Both verbal and written sign-out should follow a standard template containing structured information, with as little transcription of information as possible. Good sign-out should also allow for clarification and challenging of transmitted information, particularly around decision-making. Finally, the setting for the sign-out should be quiet and free of distractions and interruptions.

Patient handoff management is rarely taught systematically. The following principles can help to redress this, and should be considered a 'starter set' of principles to be customised based on the specific contexts of ICUs, teams and individuals as described above:

- Teach providers to tell a "better story". More effective integration of the quantitative outcomes data with the more qualitative contextual data will enhance the wisdom of health professionals, and capture the complexity of patient stories.
- Provide feedback. Sustain the effort by giving feedback about individual performance and by setting performance expectations.
- Couple inexperienced providers with experienced incoming and outgoing providers. The experienced incoming provider can demonstrate proper inquiries about patient status and issues, and the experienced outgoing provider can demonstrate proper "story-telling" and methods. Capturing the wisdom of an 8 or 12-hour shift is more complex than one might assume.
- Consider the use of videotaped simulated handovers and self-directed videotaping for reflective learning. Use of these tools can improve handover. They can demonstrate the nature of false assumptions and omissions; the effects of interruptions; good versus poor patient problem descriptions; and the consequences of relying only on written information.
- Educate all staff using interactive methods on the importance of effective handoffs and about the characteristics of good handoff – include communication training using a program such as TeamSTEPPS (Payne et al. 2012) or other team training programmes.
- Provide staff with laminated reminder cards listing desirable features of handoffs.
- Use a mnemonic such as IPASS or SIGNOUT (Li et al. 2011).
- Integrate handoffs into a team handoff instead of 'siloed' handoffs within disciplines.
- Provide a quiet private physical space for handoffs to occur.
- Perform handoffs at the bedside rather than in a conference room.
- Develop standardised written handoff tools and try to import patient information automatically from the electronic medical record into these tools (to avoid transcription errors) (Riesenburg et al. 2009; Solet et al. 2005).

The Future

Several key understandings have emerged about the complex nature of patient handoffs in the ICU. First, there is a need for a deeper understanding about how variations in communication, culture, and technology used by healthcare professionals in medicine and nursing lead to ineffective or suboptimal handoffs. Second, is the need to develop a "common conceptual ground" among all parties (individuals, teams, ICUs, wards) involved in handoffs. Third, is the recognition that interventions to improve handoffs benefit from ICU staff involvement, which increases sensitivity to local and participant context, promotes trust and enhances clinician uptake and buy-in through a shared understanding of the strengths and limits of the proposed interventions. Fourth, is the recognition that any comprehensive strategy to improve handoffs should include an evaluation of benefits, risks and cost-effectiveness, that may include the use of surrogate upstream outcomes and Bayesian methods (Taylor et al. 2011).

Further research and funding are needed to identify effective educational and workplace interventions to improve ICU handoffs. Such interventions are likely to be successful if they are multi-layered, and involve multiple stakeholders, ranging from the individual patient, clinician and clinical level, with a special focus at the microsystems and organisational levels (Toccafondi et al. 2012). Ultimately, achieving the ideal handoff on an ICU patient requires the individual clinicians and health systems to recognise the importance of good communication as a powerful therapeutic tool, one that is as important to the outcomes of ICU patients as the medications, technology, invasive procedures and surgical interventions that they receive. ■

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

Box 1

Key Messages

- Identify the leadership required to improve handovers.
- Seek to understand handover communication as a complex adaptive process.
- Recognise the effect of culture as a key enabler for change and improvement.
- Develop tools to make information readily accessible and trans parent.
- Apply principles of human factors to clinical design.
- Focus on training, assessing uptake and success and sustaining gains.

Source: Johnson and Barach 2009

Box 2

Questions to help guide local implementation of new handoff strategies and to measure the impact of the changes

- What are the clinical handoff situations that carry the most risk for patients?
- What information and critical success factors are needed to better under stand the process of handoff in this setting?
- What handoff interventions are the most effective?
- What resources and tools are available to improve handoff communication?
- Which individual clinicians are willing to serve as "champions" for improving the handoff process?
- What mechanisms can be put in place to spread, sustain and transfer improvements across the organisation?
- What improvements can be built into information systems tools to enhance their successful adoption (eg, checklists, reminder systems, information technology solutions)?

Source: Johnson and Barach 2009

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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.
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THE ROLE FOR BIO-ELECTRICAL IMPEDANCE ANALYSIS (BIA) IN CRITICALLY ILL PATIENTS

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The impact of a positive fluid balance on morbidity and mortality has been well established. However, little is known about how to monitor fluid status and fluid overload. This article discusses the different parameters related to bio-electrical impedance analysis (BIA) and their use to monitor fluid status and to guide fluid management in critically ill patients.

Introduction

Bio-electrical impedance analysis (BIA) measures whole body (or regional) impedance, phase angle, resistance, reactance and capacitance, by means of an electric current transmitted at different frequencies (Bioelectrical impedance analysis 1994; Plank et al. 1995). New techniques allow measurement of total body water with separation into extracellular and intracellular water (Janssen et al. 1997). Previous and some recent data suggest that BIA may provide useful information not only in different well-established patient groups (dialysis, AIDS, malnutrition), but also in critically ill patients with burns, trauma and sepsis undergoing fluid resuscitation (Van Biesen et al. 2011; Wabel et al. 2009; Wabel et al. 2008; Plank et al. 2000; Savalle et al. 2011; Kraemer 2006; Kraemer et al. 2006; Streat et al. 1985).

> "The recommendations for fluid monitoring can at best be described as open for discussion and debate"

BIA principle

BIA allows calculation of body composition and volumes by means of a current going through the body considered as a cylinder (see Figure 1, page 16). Details of the principles can be found elsewhere (Bioelectrical impedance analysis 1994; Foster and Lukaski 1996; Kyle et al. 2004a; 2004b). In order to obtain reproducible measurements BIA has to make five assumptions: 1) the human body can be considered as a cylinder; 2) this cylinder consists of five smaller cylinders (one central cylinder and two arms, two legs); 3) body composition is assumed to be homogenous; 4) with absence of individual variation, and 5) without impact of environment (temperature, stress, infusions…). This of course only holds true in an ideal situation that may differ from real life situations, especially in the critically ill. To obtain a good BIA measurement five factors are indispensable: impedance value, height, weight, gender and age. Of these gender and age are the most important in obtaining the highest level of accuracy. BIA allows a four compartment body composition analysis dividing the body into fat, water, mineral and protein components (see Figure 2, page 16)(Foster and Lukaski 1996).

BIA Measurement

Reproducible measurements can be obtained with tetrapolar electrodes with two current electrodes (to drive electricity into the human body) and two detection electrodes (to detect impedance) placed on hands and feet. Tetrapolar techniques provide more reproducible results (Kyle et al. 2004; 2004b). Modern devices also apply multiple frequencies, further improving the reproducibility and accuracy of the results. The frequency is the number of repetitions per second of a complete electric waveform (1 repetition per second is 1 Hz)(Plank et al. 1993; Janssen et al. 1997; Streat et al. 2000). A current with a frequency below 100 Hz will not pass the cell membranes and as such will measure only extracellular water (ECW). Current frequencies above 100 Hz will go through cells and measure total body water (TBW). The intracellular water (ICW) can then be calculated as TBW minus ECW. When electric current passes a cell membrane a time delay occurs, expressed as phase angle. A phase angle of 0 degrees is an indicator of absence of cell membranes, whereas 90 degrees represents a capacitive circuit which consists of only membranes with no fluid. The greater the number of cell membranes the signal has to pass

through, the longer the time delay. A high phase angle hence is consistent with high reactance and a large amount of waste cell membrane and body cell mass (BCM) as seen in healthy individuals, whereas (critically ill) patients tend to have a low phase angle (see Figure 3,page 16)(Savalle et al. 2012; Kyle et al. 2002). Pitfalls one has to take into account during BIA measurement are changing posture (best position being supine), incorrect position of arms (should be next to body), incorrect contact with the electrodes and contact with another person or object during measurement. Other factors that may interfere with BIA measurements that are currently not yet well understood are: infusions with large amounts of normal saline, peripheral oedema, changes in ambient air and skin temperature, sweating, conductance of hospital bed, etc.

BIA Parameters

Table 1 lists the different parameters that can be obtained with BIA. Absolute measurements of impedance, reactance, resistance and capacitance have been highly correlated to changes in the human body, and have been shown to be good prognostic indicators. Under- and overestimation of dry weight is important, and has been shown to impair the survival and quality of life of haemodialysis patients. Body composition and nutritional assessment of children and adults in clinical settings is important in order to identify potential causes of inadequate nutrition status, including the risk of malnutrition. Performing nutritional assessments in diseased patients enables medics to identify related disorders and to monitor the effects of treatment. The glomerular filtration rate (rate at which waste is removed from our kidneys) is an important indicator of kidney function. Creatinine estimations can also be performed. BIA can obtain information on minerals (bone, soft tissue) and protein content of the body. In some patients assessment of the loss of minerals can be very important. Glycogen mass is the primary storage form of carbohydrates found in the cytoplasma of most cells. Intracellular and extracellular body fluid status in both healthy and diseased patients is of significant importance. Extracellular water (ECW) increases in different diseases and oedema is the most common sign of ECW expansion. Body cell mass (BCM) is an accurate method of establishing a healthy subject's nutritional status or a patient's degree of malnutrition.

Validation

Although BIA is a simple, noninvasive, rapid, portable, reproducible, and convenient method of measuring body composition and fluid distribution, it is still unclear whether it is sufficiently accurate for clinical use in critically ill patients (Aghdassi et al. 2001). BIA measures TBW and as such it needs to be validated through comparison with other means of determining TBW or methods (such as densitometry) used to derive the components of the two-compartment model of the body composition, namely fat free mass and body fat. Because BIA disproportionately considers the extremities, the relationship between impedance and TBW can only be empirical (Bioelectrical impedance analysis 1994). This relationship probably exists in most normal subjects and in those with mild disease perturba-

tions such as mild-to-moderate obesity and other chronic illnesses not producing local fluid accumulation.

The gold standard techniques for measuring body composition and TBW are isotope dilution (labelled deuterium), followed by dual energy X-ray absorptiometry (DEXA), underwater weighing, and air-displacement plethysmography. Abdominal and visceral fat can also be measured with CT and MRI. Previous studies showed varying results and in some cases BIA could not provide additional information (Plank et al. 2005; Beshyah et al. 1995; Bracco et al. 1996; Genton et al. 2002). Total body potassium (TBK) has been found to be linearly correlated with body cell mass (BCM) (Beshyah et al. 1995). Portable methods consist of infrared, skinfold caliper, and dual contact BIA. Tetrapolar BIA falls in between basic and advanced methods. Different studies compared BIA with DEXA showing good correlation. For clinical purposes two devices are available to be used in (critically ill) patients: the Fresenius Medical Care (BCM) Body Composition Monitor (Fresenius Medical Care, Bad Homburg, Germany) (http://www.bcm-fresenius.com/index.html) and the Maltron BioScan 920 (Maltron International Ltd, Rayleigh, Essex, UK) (http://www.maltronint.com/products/bioscan920-2S.php). However, no head-to-head comparison has been performed in a large sample of critically ill patients.

Clinical Applications

As suggested by ESPEN: "BIA is an important clinical tool for evaluating the metabolic status of ICU patients. It is inexpensive and noninvasive, and it provides useful information concerning altered body composition and membrane potential at the tissue level measured by phase angle, as well as fluid imbalance" (Kyle et al. 2004a; 2004b). From a theoretical point of view the clinical applications for BIA could be numerous: AIDS, muscle wasting, anorexia, postmenopausal women, obesity, pregnancy, Crohn's disease, cystic fibrosis, diabetes, paediatric diseases, enteral and parenteral nutrition, elderly, rheumatoid disease, tropical disease… BIA can be helpful in burn patients, cardiovascular disease, peripheral oedema, gastroenteritis, haemodialysis, CVVH, liver disease, second and third spacing (segmental analysis), lung disease, ARDS, malnutrition, bariatric surgery, postoperative fluid status, renal failure, stroke…

BIA can detect changes in body composition even in the early stages of kidney disease and in patients with cardio-renal syndromes, showing lower resistance, abnormal impedance vectors, reduced phase angle, and higher total body water together with a lower body cell mass. Importantly, patients do need to have overt signs of overhydration or malnutrition for BIA to detect these alterations (Bellizzi et al. 2006; Aspromonte et al. 2012). These changes in body composition continue during the entire spectrum of chronic kidney disease, being most evident in end-stage renal disease (Dumler and Kilates 2003). In chronic haemodialysis patients multifrequency whole body BIA can give an objective measure of fluid and nutritional status, calculating overhydration within one to two litres (Tattersall 2009). Using BIA as a guide to achieving dry weight results in an improved fluid status and control of blood pressure (Moissl et al. 2013). In peritoneal dialysis patients, who often have a significant residual kidney function, BIA guided fluid management (with measurements performed after draining the intraperitoneal cavity (Arroyo et al. 2014) can help restore diuresis in underhydrated patients and improve tension and weight control in overhydrated patients (Van Biesen et al. 2011; Crepaldi et al. 2009).

Many conditions exist in critical illness (ascites, anasarca, severe peripheral oedema, pleural effusions, the massively overhydrated patient…) where conventional BIA may only provide a poor measure of TBW (Kyle et al.2004a; 2004b). Therefore, for the time being BIA can only be considered as a research tool in critically ill patients because the TBW-to-FFM ratio is variable and the body impedance-to-TBW ratio may often vary during the above-cited conditions (Bioelectrical impedance analysis 1994; Kyle et al. 2004a; 2004b).

It is important for the clinician to be aware that the normal ECW/ICW ratio is less than 1. Critically ill patients, especially those with severe sepsis, are prone to develop changes in body fluid distribution with migration of fluid from the intravascular to the extravascular space. Furthermore, the systemic inflammatory response produces changes between the FFM and TBW distribution (Harrison 2010). Raw impedance data can provide information on hydration and cell mass integrity (Barbosa-Silva and Barros 2005).

Plank found that although changes in TBW were similar, patients with peritonitis and sepsis (n=12) had higher ECW values compared to those with blunt trauma (n=18) (Plank and Hill 2000). In a study on the use of continuous veno-venous hemofiltration to adjust fluid volume excess in 30 septic shock patients with AKI Dabrowski and co-authors found a sustained increase in nonsurvivors (Dabrowski et al. 2014). A similar study in 68 ICU patients with sepsis (n=51) compared to patients without sepsis (n=17) showed that ECW and FFM hydration were increased in severe sepsis compared to sepsis (Słotwiński et al. 2013). Changes in tissue physiology and integrity during sepsis may produce changes in electrical properties, as such; the use of raw data obtained with BIA seems promising. Indeed, raw data are not influenced by assumptions that can affect body composition results, and bio-electrical impedance vector analysis provides information on tissue hydration and BCM independent of regression equations, even in overhydrated patients (Nwosu et al. 2013). The study by Słotwiński showed that patients with sepsis had significantly higher raw impedance (566±98.66 Ω vs. 423.86±149.7 Ω; p=0.0003) and resistance normalised by height (336.69±66.9 Ω/m vs 259.94±90.9 Ω/m; p=0.00165) than those with severe sepsis (Słotwinski et al. 2013). The lower mean phase angle of the patients with sepsis laying above 50th percentile in the study by Słotwiński could be related to a low body cell mass and high ECW/ICW ratio, as observed by other investigators (Buffa et al. 2013). A retrospective study comparing BIA data from critically ill patients (n=15) with healthy volunteers (n=25) showed significant differences in body water composition between patients and healthy individuals (Huygh et al. 2013). In this study patients had higher values for TBW (45±7.7 vs 38±9.7 Ltr, p=0.01), ECW (24.1±5.4 vs 16.9±5.3 Ltr, p<0.0001) and ECW/ICW ratio (1.2±0.2 vs 0.8±0.2, p<0.0001) while ICW was lower 20.9±3.8 vs 21.2±5 Ltr, p=NS) (Huygh et al. 2013).

Conclusions

BIA is non-invasive and relatively inexpensive. BIA can be performed at bedside, and does not expose to ionising radiation. Modern devices have very limited between-observer variations. However, BIA parameters are population-specific and one must be aware of clinical situations that may interfere with the measurement. BIA allows assessment of TBW, ICW, ECW, ECW/ICW ratio and calculation of volume excess. As such it can help to guide de-resuscitation in patients not transgressing spontaneously from the Ebb to Flow phase of shock (Cordemans et al. 2012). More research is needed in critically ill patients before widespread use of BIA can be suggested in critically ill patients.

Acknowledgements

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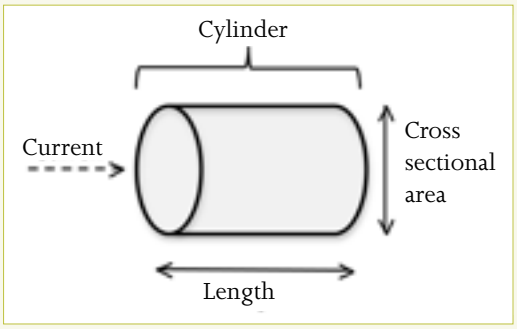
Table 1. Different Parameters That Can Be Obtained With BIA

ABSOLUTE MEASUREMENTS
• Impedance
• Phase Angle
• Resistance
• Reactance
• Capacitance
DRY WEIGHT
• Dry Weight
BODY COMPOSITION
• Fat %
• Fat Mass
• Fat Free Mass
• Fat Free Mass %
• Body Volume
• Body Density
• Body Mass Index
• Resting Metabolic Rate
• Target Fat (min / max) %
• Target Weight (min / max)
• Target Water (min / max) %
KIDNEY FUNCTION
• Glomerular Filtration Rate
• Creatinine
MINERALS AND PROTEIN
• Total Body Potassium
• Total Body Calcium
• Protein Mass
• Mineral Mass
GLYCOGEN
• Glycogen Mass
FLUID STATUS
• Extracellular Fluid
• Intracellular Water Volume
• Extracellular Water Volume
• Total Body Water Volume
• Intracellular Water Lt, %
• Extracellular Water Lt, %
• Total Body Water Lt, %
• Extracellular Mass
• Extracellular Solids
• Extracellular / Intracellular Water
• Extracellular Water / Total Body Water
• Intracellular Water / Total Body Water
• Interstitial-Fluid Extravascular
• Plasma-Fluid (Intravascular)
NUTRITIONAL STATUS
• Body Cell Mass
• Muscle Mass

Figure 1. BIA Principle
When electric current goes through a cylinder-shaped body the impedance (Z) is related to the length (L) and specific resistivity (ρ) of the tissue and inversely related to the cross-sectional area (A) of the cylinder. The volume of a cylinder (V) can be calculated as L multiplied with A.



How does bioelectrical impedance analysis calculate volumes?

$Z = \rho . LA$

$Z = \rho . LA . LL$

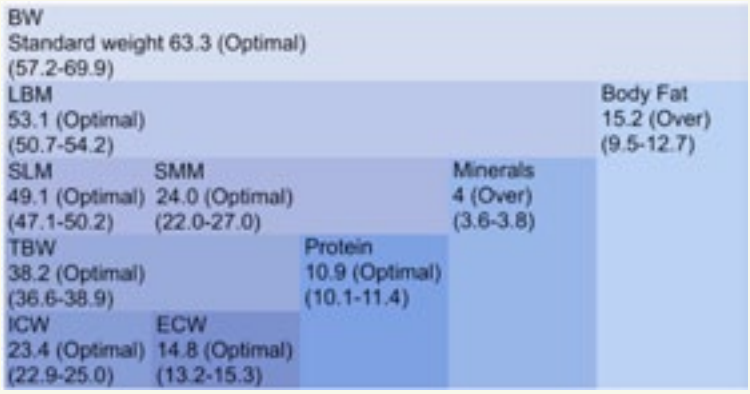
$Z = \rho . L2V$

Extrapolated to a patient, L stands for the height (in cm) so that the body composition and volume (V) can be calculated as follows:

$V = \rho . L2Z$

where L2Z corresponds to the impedance index that can be calculated with bioelectrical impedance analysis

Figure 2. The Four Compartment Body Composition Analysis With BIA



ICW: Intracellular water (body water that exists inside the cell membrane)
ECW: Extracellular water (body water that exists outside the cell membrane Ex tracellular can be further subdivided into interstitial, lymphatic, trans-cellular fluid and blood)
TBW: Total body water = ICW + ECW (Body water that exists in- and outside of cell membrane)
SLM: Soft lean mass = total body water + protein (Skeletal and smooth muscle maintaining body function)
SMM: Skeletal muscle mass
LBM: Lean body mass = SLM + minerals
BW: Body weight = LBM + body fat

The values in between () are the range of standard body composing constituents. Units are expressed in Litres.

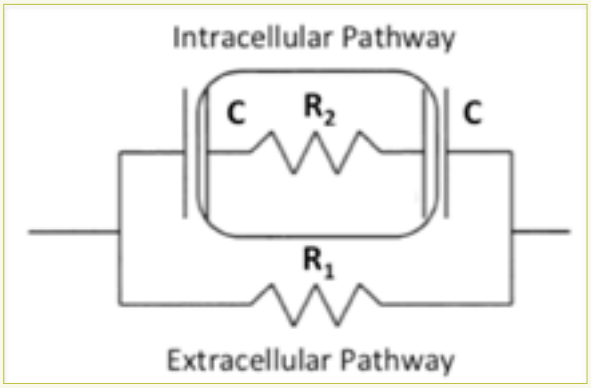
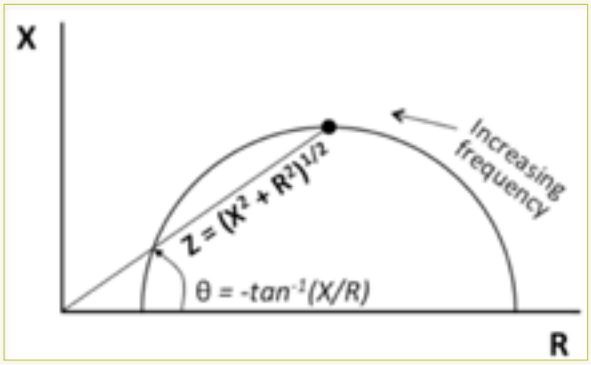


Figure 3. BIA Principles
Panel A. Biological tissues act as conductors or insulators and the flow of current through the body will follow the path of least Resistance (R). Fat Free Mass (FFM) contains large amounts of water and electrolytes and therefore is a better conductor of electrical current than fat and bone, which are poor conductors as they contain low amounts of fluid and conducting electrolytes. The cell membrane of a body consists of a layer of non-conductive lipid (fat, oils and other lipid like substance) material sandwiched between two layers of conductive protein molecules. Cell membranes become reactive elements behaving as capacitors (C) when electrical current is applied.



Panel B. With BIA the Phase angle (θ), the Reactance (X) and the Resistance (R) are measured. Normal Phase angle is 4-15°. Adapted from Foster and Lukaski.

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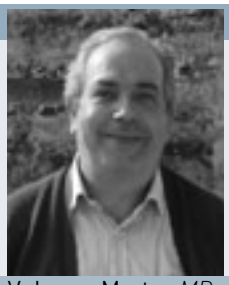
CARE OF THE MULTIPLE ORGAN DONOR



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The precise care of the multiple organ donor can reverse the derangements resulting from previous disease and brain death, stabilise the donor and help to obtain more and better functioning organs.

Introduction

Several diseases (cerebral haemorrhage or infarction, meningitis) or conditions (head trauma) can lead to severe intracranial hypertension and global ischaemia and thus to brain death (BD). Once this has been certified, absolute / relative contra-indications to organ donation must be excluded and /or considered. Having done this, if according to the local laws there is no obstacle for the donation, the process can start. It's time for the Transplant Coordinator to start work that will end not only with the extraction of the organs, but after the transplant to the recipients and the recovery of their function.

Once BD has been established, the potential donor must be actively monitored and treated, not just considered as a corpse that awaits the extraction process and left to spontaneous evolution. After hours or days of fight against the progressive deterioration primarily of the brain and other organs, care of the donor must focus on the support, protection and treatment of the deranged organs considered for transplant. This has been termed "targeted donor treatment". Knowledge of the physiopathological changes that accompany BD is crucial in order to delay or fight effectively against them (Power and Van Heerden 1995). Some brain-dead potential donors will go into an irreversible cardiac arrest shortly after the acute process of BD, irrespective of the treatments started.

The cardiovascular and respiratory systems show the most severe changes, but endocrine or metabolic changes can also be detected. Their adequate management will be key to correcting and preserving organ function and viability (Valero 2002). The more time elapsed since BD the more intense the degree of instability of the donor (Mascia et al. 2009), so the duration of the process from BD until organ extraction is important in order to get more and better organs, (as shown by Venkateswaran et al. (2008) and Cantin et al. (2003), for lungs and hearts).

Several years ago, inadequate donor management resulted in the loss of a high number of potential donors, due to cardiovascular collapse before organ extraction. Donor management programmes can reduce this loss (Salim et al. 2006). Great efforts have been made in this field, resulting in standardised protocols and detailed algorithms that should be used universally (Valero 2002; Salim et al. 2006; Shemie et al. 2006; Rosendale et al. 2002; Jenkins et al. 1999; Lopez-Navidad et al. 1997; Wood 2006). In addition, the progressive specialisation of the doctors charged with the donor's care has improved the results in terms of organs extracted and their functionality (Wheeldon et al. 1995).

Several models of organisation, such as the Spanish Model (Matesanz 2008, Manyalich 2011) and Transplant Coordinators' training (see Transplant Procurement Management Courses [www.tpm.org]), have been used successfully for more than 25 years and can be considered cornerstones of this practice. Initiatives such as the European Transplant Coordinators Organisation's Certificate of European Transplant Coordination (CETC)/ETCO [www.etco.org]) are basic to accredit the knowledge, training and experience of transplant coordinators, providing certification for an internationally recognisable level of expertise.

The different attitudes and demands of the surgical groups involved in the process of organ extraction and transplantation can influence the work of doctors charged with the care of these patients. One group can perhaps request the avoidance of inotropes; while another can seem not to be concerned at all by them, or there can be opposite opinions regarding the fluid balance in the donor. But one thing must be always kept in mind: the primary goal of donor management is to improve organ function, overcoming the physiopathological derangements caused by brain death, and to obtain as many viable and well-functioning organs as possible. This is a global view, not a single-organ focused view.

Cardiovascular Problems Monitoring

Apart from a continuous ECG and SpO_2, invasive monitoring of the donor is mandatory. An indwelling arterial catheter is necessary to monitor closely arterial pressure, and to obtain repeated samples to determine blood gases and acid-/base status. Although central venous pressure (CVP) values are usually close to pulmonary capillary wedge pressure (PCWP), in cases of left ventricular dysfunction CVP may remain low despite high PCWP values (Powner and Crommett 2003). In cases of haemodynamic instability and cardiac dysfunction (ejection fraction < 45%), a pulmonary artery catheter will help to measure left ventricular filling pressure and cardiac output, to guide the administration of vasoactive drugs or to adjust the fluid balance (Wood et al. 2004.) When haemodynamic management is difficult (no response to usual measures, previous heart disease, etc.), other invasive cardiovascular monitoring systems, such as PICCO or Vigileo devices, and transthoracic or transoesophageal echocardiography can be useful (Gu et al. 2009).

Recently, monitoring of mixed venous oxygen saturation (aiming at SvO_2 values between 60-80%) has been proposed in potential organ donor patients. It could detect early changes

in the patient's condition, allowing earlier interventions. (Shemie et al. 2006) The monitoring of base excess and lactate levels has been shown to be efficacious to guide fluid administration and resuscitation (Dominguez-Roldan et al. 2005).

Haemodynamic Disturbances

Two phases can be differentiated during the process of brain death: the first characterised by a massive sympathetic discharge and the second by a severe reduction of sympathetic tone. The first one can be qualified as a 'storm', with an acute elevation of blood pressure (often to extreme values) and other acute and severe cardiovascular disturbances. This can be followed shortly after by a severe episode of hypotension (loss of vascular tone) and reduction of cardiac output due to a disturbance in the inotropic and chronotropic status of the heart (Avlonitis et al. 2005). In the first phase (lasting from minutes to hours), the findings are arterial hypertension, bradycardia that later progresses to supraventricular tachycardia and/or ventricular extrasystoles, changes in the ECG (ST-segment elevation) and hyperthermia. This period can be really difficult to manage. Some studies advocate the short-term use of beta-blockers such as esmolol, which would mitigate this hypertensive and arrhythmogenic response during cerebral herniation. In another study, esmolol, administered before BD, helped to preserve myocardial function (McLean et al. 2007). In donors in this phase, the treatment of hypertension with esmolol and urapidil seems to increase the number of viable heart grafts (Audibert et al. 2006).

After this, there is a dysfunction (or destruction) of the vasomotor centre, and the release of catecholamines is reduced. Vasodilatation and reduction of the peripheral vascular resistance ensue (Wood et al. 2004). Previous restriction of fluids, plus a multifactorial polyuria (ADH deficiency, hyperglycaemia, use of mannitol, hypothermia), lead to progressive hypovolaemia and worsen the hypotension.

The derangement in cardiac function is multifactorial (hormonal deficiency involving free thyroxin, cortisol, arginine -vasopressin and insulin; increase in the anaerobic metabolism). The result is an alteration of inotropism and chronotropism, with a subsequent drop in cardiac output. Some authors (Salim et al. 2006, Shivalkar et al. 1993) have described some degree of cardiac ischaemia in nearly 30% of donors.

The goals of optimal haemodynamic management of the donor must be the maintenance of an adequate circulating volume, a normal cardiac output and a good perfusion pressure to achieve optimal oxygen supply to the tissues. An adequate perfusion pressure in the donor is crucial for the viability and function of the transplanted organs. Diverse experiences show that a systolic arterial pressure over 100 mmHg must be the objective. Although controversial as an effective measurement of the cardiac filling pressure there is an agreement to recommend a target value of CVP of between 10 and 15 cm H_2O in the donor.

With adequate management, cardiac function can recover after several hours, as demonstrated by several works (Casartelli et al. 2012; Christmas et al. 2012).

Cardiac Arrhythmias and Conduction Disorders

These appear in 20-30% of donors. Sinus tachycardia is the most common, (20-50%), followed by sinus bradycardia (15%) and auricular fibrillation (10%) (Powner and Allison 2006).

Bradycardia appears often, usually as part of the Cushing phenomenon (hypertension and bradycardia). After BD, the nucleus ambiguous of the brain stem is destroyed and vagal tone is lost; therefore atropine will not be capable of reversing the bradycardia. Drugs with a direct chrono-

tropic effect must be used instead. Isoproterenol (1-3 µg/min) is the most effective. Dopamine, dobutamine and epinephrine also have a positive chronotropic effect.

Other types of ventricular and auricular arrhythmias as well as conduction abnormalities are also seen. The usual causes are electrolyte imbalance, hypothermia and myocardial ischaemia, but also iatrogenic (infusions of inotropic drugs, etc.), or can be of a central origin. The aetiological treatment should be applied first and, if proven insufficient, antiarrhythmic drugs should be used, amiodarone being the first choice (Powner and Allison 2006). In cases of refractory ventricular arrhythmias, hypothermia should be considered the triggering factor, and fought against. Prolongation of the QT interval may trigger ventricular extrasystoles and "torsade de pointes"- type ventricular tachycardia. If so, all medications that may prolong the QT interval must be stopped, the electrolyte imbalances corrected, particularly hypokalaemia, and magnesium given intravenously at a dose of 2 g IV/10 min. Occasionally it can be necessary to implant a temporary pacemaker to prevent the relapse of the arrhythmia (Nolan et al. 2005). In this situation management of the donor can be extremely difficult, and can progress to an irreversible cardiac arrest, with the loss of the donor. In this case some teams are now able to preserve the organs using the perfusion techniques developed for "non-heart-beating donors" that have been described elsewhere (Valero 2002).

Replacement of Losses of Fluids and Electrolytes

The donor suffers important losses of free water and of electrolytes. Imbalances such as hypernatraemia, hypocalcaemia, hypomagnesaemia, hypokalaemia and hypophosphataemia are important for the development of cardiovascular problems, such as arrhythmias, myocardial dysfunction and sudden cardiac arrest (Wood et al. 2004).

Regarding hypovolaemia, the possible causes (frequent: ADH deficiency, osmotic diuresis, hyperglycaemia; rare: hyperthermia) and the water deficit must be adequately corrected. Hyponatraemia and hyperglycaemia can derive from an excessive administration of glucose-containing fluids. If sodium-rich solutions are used, mainly in patients with an increased osmolarity, hypernatraemia can develop, and its treatment is difficult. Hypernatraemia is a negative prognostic factor for the function of liver grafts (Cywinski et al. 2008).

Fluid replacement can be done with isotonic crystalloid (normal saline or Ringer's) and colloid solutions. The rate of infusion should be of 5 ml/kg every 5-10 minutes until a systolic BP over 100 mmHg or a CVP of 12 cm H_2O is reached. Complications of volume replacement can be pulmonary oedema, cardiac overload or hepatic congestion.

A state of normovolaemia must be attained before starting vasopressor drugs. Apart from the recent findings about colloid administration to critically ill patients (Annane et al. 2013), and taking into account that we are talking about a short-term use, third generation colloids do not seem to produce acute tubular necrosis in the recipient. That problem had been reported when larger volumes of first and second-generation colloids were used, and the glomerular filtration was impaired (Cittanova 1996). The renal effect of hydroxyethylstarch (HES) solutions remains controversial. In a retrospective and comparative study (HES 130/0.4 and HES 200/0.6), the administration of HES 130/0.4 resulted in lesser incidence of delayed graft function and lower serum levels of creatinine (Blasco et al. 2008). When using a crystalloid / colloid combination, the ratio should not be higher than 65% / 35%. However, to this point there is no evidence supporting the use of hydroxyethil starch in brain-dead or other critically ill patients (Gattas 2012).

> **"Care of the donor must focus on the support, the protection and the treatment of the deranged organs considered for transplant"**

Adequate oxygenation must be ensured by maintaining the levels of haematocrit above 30%, and of haemoglobin between 90 and 100 g/L (Zaroff et al. 2002).

Use of Inotropes and Vasopressor Drugs

Persistent hypotension after adequate volume replacement should be treated with inotropic drugs. Dopamine has been the most extensively used drug. Several studies (Schnuelle et al. 1999; 2001; 2001; 2004) suggest that the use of catecholamines in donors would reduce the rates of acute rejection and increase graft survival. The pre-treatment of donors with low doses of dopamine reduces the need for dialysis after kidney transplant without clinically significant impact on graft or patient survival (Schnuelle et al. 2009). High doses (>10 µg/kg/min) must be avoided, because, due to its action on alpha-adrenergic receptors, it can induce a progressive renal and systemic vasoconstriction, the depletion of endogenous norepinephrine and of ATP reserves in the organs, and affect their function after implantation, especially in the case of the heart. Some authors do not share this view.

Dobutamine would also be beneficial in patients with altered cardiac contractility, such as patients with low ejection fraction (EF) after BD or with a myocardial contusion.

If fluids, dopamine and dobutamine do not maintain blood pressure, then noradrenalin at a dose of between 3 and 20 µg/kg/min may be used. Noradrenalin at low doses is included in some protocols as the vasoactive drug of first choice, since in many ICUs it has replaced dopamine for that indication.

A recent meta-analysis (De Backer 2012) in septic shock patients favours the use of noradrenalin, because dopamine was associated with greater mortality and higher incidence of arrhythmias. The use of drugs with a predominantly vasoconstrictor effect (ephedrine, methoxamine) should be avoided when possible. Where it is available, vasopressin has become the drug of first choice for the treatment of organ donors requiring vasoactive support. Several authors have described its successful use and the catecholamine-sparing effect (Kutsogiannis et al. 2006; Pennefather et al. 1995). Vasopressin has demonstrated a stabilising effect on systemic BP after brain death, and an effect in diabetes insipidus, which appears in 80% of brain dead donors (Venkateswaran et al. 2009).

When the appropriate BP cannot be attained, the previous treatments may be replaced by an infusion of adrenaline at low dose (0.1 µg/kg/min). Renal function must be carefully maintained, with a strict control of diuresis. Maintenance of an adequate perfusion pressure with the use of vasopressors and mannitol or furosemide has been used to protect the kidneys.

Respiratory Problems

Up to 15% of all donors show simultaneously an acute respiratory distress syndrome (ARDS) or an acute lung injury (ALI) (Mascia et al. 2006). After BD, especially in young individuals, a neurogenic pulmonary oedema may appear, due to the abrupt increase of circulating catecholamines. Several physiopathological mechanisms can be implied. The catecholamine storm produces an alteration of capillary permeability, together with haemodynamic changes that produce an increase

in hydrostatic pressure and damages to the alveolar-capillary membrane. Also, the activation of inflammatory mediators by the cerebral and organic ischaemia and the endothelial activation will have profound effects on the pulmonary function (Avlonitis et al. 2003).

Ideally, arterial pO_2 should be kept above 100 mmHg, with the lowest FiO_2 possible and the lowest level of Positive End Expiratory Pressure (PEEP). The low CO_2 production, due to the absence of cerebral blood flow, and to the loss of sympathetic activity and muscular tone, requires the use of minute volumes lower than those currently used with the aim of maintaining normocapnia. In lung donors it is extremely important to follow standardised protocols to optimise and maintain optimal lung function (Powner et al. 2000). The management of these patients should include: the use of low FiO2 to avoid pulmonary toxicity (less than 60%), the general use of PEEP (8-10 cm H2O) to reduce atelectasis, the avoidance of an excessive fluid overload with close monitoring of the values of central venous, pulmonary and pulmonary capillary wedge pressures, the adequate use of inotropic agents (and/or vasopressin), and preventive measures against respiratory infections. As in any critically ill patient, the close monitoring of respiratory function, the use of alveolar recruitment manoeuvres, the early and precise diagnosis of respiratory infections using flexible bronchoscopy (Riou et al. 1994), plus bronchoalveolar lavage or the protected-specimen brush technique, as well as the use of protective ventilation (6 to 8 mL/kKg of ideal body weight, and PEEP of 8 to 10 cm H2O), improve lung function in the donor and the number of potential organs for transplant (Mascia et al. 2010). A closed circuit should be used for tracheal suction. The apnoea test should be performed with the ventilator in continuous positive airway pressure (CPAP) mode, and recruitment manoeuvres are recommended after any disconnection from the ventilator. An aggressive protocol aimed at improving the obtention of lungs for transplant is not deleterious for other organs (Minambres et al. 2013).

The systemic inflammatory response and lung damage due to an inadequate mechanical ventilation setting (volutrauma and barotrauma) may exacerbate the organ damage due to inflammatory mediators (Mascia et al. 2006). Methylprednisolone at doses of 15 mg/kg has been demonstrated to improve the gas exchange and is an independent predictor of successful lung transplant (Follette et al. 1998)

Control of Temperature

This is another crucial point in the management of the organ donor. After BD, the hypothalamic control of temperature is lost, and the donor becomes poikilothermic. The loss of body heat leads to deterioration of the haemodynamic state by vasoconstriction and cardiac instability. Hypothermia also induces arrhythmias (general delay of conduction, inversion of T wave, QT lengthening, appearance of Osborn J wave [between 32-33ºC], atrial fibrillation, and ventricular fibrillation with temperatures lower than 30ºC), disorders of renal function due to the reduction of glomerular filtration and the incapacity to maintain tubular concentration gradients (cold diuresis), coagulation disorders and a left shift of the oxygen-haemoglobin dissociation curve with a reduction of free oxygen delivery to the tissues.

Treatment consists of heated intravenous solutions, the humidification and heating of respiratory gases, as well as the use of insulating or warming electric blankets to maintain the body temperature above 35ºC.

Endocrine Disorders

Diabetes Insipidus

Diabetes insipidus is common in BD, (occurring in 38% to 87% of cases (up to 98% in some series), and is due to a deficiency of anti-diuretic hormone (ADH). There is a loss of hypothalamic-pituitary control over ADH secretion and release, [in response to osmotic stimuli (sodium concentration) on the hypothalamic osmoreceptors and to other non osmotic stimuli from receptors of cardiac and pulmonary volume that are integrated in the hypothalamus]. A few hours after BD, plasma levels of vasopressin are not detectable (<0.1-0.5 pg/ml). This results in an uncontrolled increase in the production of hypotonic urine (diuresis >4 ml/kg/h; density <1005; plasma osmolarity >300 mmol/kg and urinary osmolarity <300 mmol/kg) and subsequent hypernatraemia, hypomagnesaemia, hypokalaemia, hypocalcaemia and hypophosphataemia. These losses should be treated with fluids and the adequate ionic supplements. When urine production exceeds 200-250 ml/h (3-4 ml/kg/h) ADH analogues should be administered.

At low doses (1-2 U/h; 2-10 mU/kg/min), vasopressin acts on the V2 receptors of renal cell membranes, increasing water reabsorption and reducing diuresis, while at higher doses it acts on the V1 receptors of blood vessels, producing arterial hypertension and vasoconstriction in the pulmonary, mesenteric, hepatic and coronary territories, and reducing renal flow without increasing its effect on diuresis. Its duration of action is close to 2-3 hours and should preferably be administered as continuous infusion. The recommended dose is 5-10 IU [units] of subcutaneous or intramuscular vasopressin sc or im every 2-4 hours or an infusion of 10 IU in 500 ml of saline at a rate of 50 ml/h.

Desmopressin (dDAVP, 1-deamino-8- D-arginine vasopressin), is a synthetic analogue of natural hormone (arginine vasopressin), and has a selective action on V2 receptors with a powerful anti-diuretic effect (anti-diuretic / pressor ratio = 2.000 to 3.000:1), so is the drug of choice. The latency time is 15 to 30 minutes and is more powerful and long acting (5-12 hours). It can be administered as an intravenous bolus of 0.03- 0.15 µg/kg/8-12 hours or 1-5 µg/8-12 hours. Subcutaneous or intramuscular administration should not be used due to the erratic drug absorption depending on the haemodynamic status and temperature. The use of desmopressin was not associated with better kidney graft outcomes in a recent meta-analysis (Rech 2013). Nevertheless, it is safe and useful to limit the harmful effects of profuse polyuria, decreasing the need to infuse large volumes and preventing haemodynamic collapse (Dictus 2009).

Other Endocrine Disorders

The consequences of BD on the anterior pituitary are not fully elucidated. Triiodothyronine levels are decreased, and do not respond to the exogenous administration of thyrotropin-releasing hormone (TRH). After BD, aerobic metabolism is gradually replaced by anaerobic metabolism, leading to progressive metabolic acidosis, increased lactate levels, and haemodynamic instability. The administration of T3 promotes a rapid increase of Ca++, ATP, glucose, and pyruvate levels, together with a reduction of the production of CO2 and the normalisation of lactate levels. Those findings would suggest the return to aerobic metabolism, the replenishment of cell energy reserves and an improvement in the myocardial function and the haemodynamic status of the donor (Garcia-Fages et al. 1993; Novitzky et al. 1988; 1990; 1991). Other authors suggest that the findings could correspond to a "sick euthyroid syndrome" and, in some cases, argue against the use of hormonal therapy in patients with severe brain damage. The previously described results have not been reproduced and T3 is not widely used. A recent meta-analysis did not find any benefit of triiodothyronine replacement on donor heart function (Macdonald 2012).

However, the use of hormone "cocktails" in donor management is gaining acceptance acceptance in some countries (Rosendale et al. 2003; Shemie et al. 2006). One paper described the use of triiodothyronine, arginine vasopressin, methylprednisolone and insulin as part of a general protocol of donor management, but with poor results (Rosendale 2002). Other authors recommend the use of hormone replacement therapy only in unstable donors requiring dopamine doses >10 µg/kg/min or with an ejection fraction lower than 45% (Wood 2004). Treatment with hydrocortisone or even fludrocortisones could result in better outcomes in terms of haemodynamic stability and reversal of relative adrenal insufficiency, but has not been widely used nor been the object of controlled trials (Rech 2013).

> **"The primary goal of donor management is to improve organ function… and to obtain as many viable and well-functioning organs as possible"**

Hyperglycaemia

Common causes of hyperglycaemia are the high levels of adrenal hormones, the administration of glucose-containing solutions, treatment with glucocorticoids and catecholamines, hypothermia and changes in pancreatic microcirculation. This may lead to imbalances of fluid and electrolytes, such as metabolic acidosis, osmotic diuresis, dehydration and hypovolaemia. Therefore, these parameters should be strictly controlled, administering a continuous intravenous infusion of insulin if necessary. Donor hyperglycaemia seems to be associated with lower graft survival in pancreatic transplants, but cannot be considered a contraindication for organ donation, because pancreatic function is usually not affected. The dose of rapid-acting insulin should range between 0.5 and 7 IU/hour of rapid-acting insulin (Blasé-Ibanez et al. 2009).

Coagulation Disorders

Up to 55% of organ donors may show coagulation disorders, which may even constitute a state of disseminated intravascular coagulation (DIC) (Salim et al. 2006). The brain tissue releases fibrinolytic agents (thromboplastin, brain gangliosides) from ischaemic-necrotic foci, and these can probably be the initial cause of coagulopathy and its maintaining factor (Powner et al. 2000). Coagulopathy must be aggressively treated with plasma, factor concentrates or platelets in order to maintain coagulation parameters within normal limits. Donor coagulopathy is multifactorial, and previous treatments, such as warfarin, aspirin or non-steroidal anti-inflammatory drugs and hypothermia may contribute, and must be corrected.

Infectious Complications

Lung infection can be the result of the initial event, or appear as a complication of prolonged mechanical ventilation. Furthermore, there can be different injuries that may cause localised infections, and the treatment and monitoring devices may promote the entry of microorganisms to the body, and the development of sepsis. When necessary, antibiotic prophylaxis should be started, and in case of suspected infections, adequate treatment prescribed, supported by adequate cultures. The high incidence of pulmonary infections is one of the most important factors that preclude lung donation. Adequate antibiotic treatment (ideally according to the results of Gram staining and culture of tracheo-bronchial secretions, and protected brush samples (PBS) or bronchoalveolar lavage (BAL) specimens) is crucial to avoid the transmission of the infection to the

recipient, and may facilitate the final success of the donation (after having demonstrated adequate treatment before the extraction process starts).

Future Improvements

Future research must include fighting against inflammatory and coagulation pathways (avoiding its activation, modulating the response and inhibiting the end-organ damage). The possibility of prolonged care of the donor in order to increase the number of organs obtained after a period of careful management (establishing a balance between the desired improvement in the function of some and avoiding the progressive deterioration of others, including the possibility of loss of the donor), will be a field widely explored. In such cases, some aspects, perhaps neglected nowadays, such as adequate provision of nutrients (micro and macro) will also gain relevance. The indications for organ transplants have increased with time (undoubtedly due to the success of the actual programmes), but the availability of organs is still very low, even in the countries with the most successful programmes of organ donation such as Spain (that has determined the objective of 40 donors per million inhabitants in the near future) (Matesanz et al. 2009). ■

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Two Randomized Trials Presented at the Euroanaesthesia 2014 Congress Show Similar Fluid Administration and Risk Profile with PVI as with Invasive or Complicated Procedures

Two Additional Studies Presented on Noninvasive SpHb in Postpartum Hemorrhage Detection and Oral Surgery

Four new clinical studies evaluating Masimo noninvasive patient monitoring technologies were presented at the **European Society of Anaesthesiology's** (ESA) Euroanaesthesia 2014 Congress in Stockholm, Sweden.

PVI Studies

At University Hospital Linköping, in Linköping, Sweden, researchers evaluated whether fluid volume optimization using **PVI** would lead to similar fluid management and patient risk compared to Stroke Volume Optimization using Esophageal Doppler (ED) – an established method to optimize preload during abdominal surgery. Researchers noted the ED technique "is costly and sensitive to interference, requires training and is not possible in prone position or at limited access to the head." The investigators reported that there were no differences in colloid administration, total volume of fluids given during surgery, or lactate levels at the end of surgery. Higher lactate levels are strongly associated with greater patient risk. The investigators concluded: "Fluid optimization during open abdominal surgery guided by PVI seems to result in equal amounts of fluid administered compared to guidance using ED technique."[1]

At CHU Brugmann (Brugmann University Hospital) in Bruxelles, Belgium, researchers compared conventional pulse pressure variation induced by mechanical ventilation (PPV) with noninvasive PVI to predict intraoperative fluid management in patients undergoing elective abdominal (laparoscopic) surgery. Seventy-two patients were randomized according to the monitoring used to guide intraoperative fluid therapy (PPV group: N=36, PVI group: N=36). Basal balanced crystalloid infusion rate was set at 2 ml/kg/h and boluses of 250 ml of 3% modified fluid gelatin were administered if the PPV was ›13% or the PVI ›15% in the respective groups for more than five minutes. Researchers concluded: "The type of monitoring does not influence significantly the volume of fluid administered in the intraoperative period."[2]

SpHb Studies

At Città di Roma Hospital in Rome, Italy, researchers compared noninvasive **SpHb** with values from an invasive central laboratory device (Horiba Pentra DX 120) in laboring mothers to evaluate whether SpHb (rainbow® ReSposable R2-25 Revision K sensor; **Radical-7** Pulse CO-Oximeter®) could detect changes in hemoglobin to enable earlier detection of postpartum hemorrhage. The investigators reported: "SpHb demonstrated bias and precision of 0.10 ± 0.71 g/dL compared to the central laboratory device with limits of agreement of 1.51 and -1.31 g/dL. More importantly, SpHb was able to trend changes detected by laboratory readings." They concluded that in this study: "SpHb was able to detect changes in hemoglobin concentration during and after delivery and therefore may provide a means for the early detection of bleeding and postpartum hemorrhage."[3]

At Tokyo Dental College Ichikawa General Hospital in Chiba-ken, Japan, researchers evaluated the accuracy of SpHb compared with laboratory CO-Oximetry measurements of total hemoglobin (tHb) during prolonged oral surgery. The investigators reported that 73 tHb values were compared to SpHb. Bias and precision were 0.86 g/dL and 1.17 g/dL, respectively. Bland-Altman analysis showed limits of agreement of -1.43 to 3.15 g/dl. They concluded: "The accuracy of SpHb monitoring during prolonged surgery was clinically acceptable, as shown by the low bias, precision and moderate limits of agreement when compared to laboratory values, although percent error exceeded normal range slightly."[4]

The Masimo rainbow® SET platform enables the assessment of multiple blood constituents and physiologic parameters that previously could only be measured invasively or with complicated procedures, in addition to providing Masimo SET® Measure-through Motion and Low Perfusion™ pulse oximetry including SpO_2, pulse rate, perfusion index, and PVI. Multiple noninvasive and continuous measurements – including SpHb, RRa®, SpCO® and SpMet® – offer an advancement in patient safety by helping clinicians better assess patients.

MASIMO®

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ABOUT MASIMO

Masimo (NASDAQ: MASI) is the global leader in innovative noninvasive monitoring technologies that significantly improve patient care-helping solve "unsolvable" problems. In 1995, the company debuted Measure-Through Motion and Low Perfusion pulse oximetry, known as Masimo SET®, which virtually eliminated false alarms and increased pulse oximetry's ability to detect life-threatening events. More than 100 independent and objective studies have shown that Masimo SET® outperforms other pulse oximetry technologies, even under the most challenging clinical conditions, including patient motion and low peripheral perfusion. In 2005, Masimo introduced rainbow Pulse CO-Oximetry technology, allowing noninvasive and continuous monitoring of blood constituents that previously could only be measured invasively, including total hemoglobin (SpHb®), oxygen content (SpOC™), carboxyhemoglobin (SpCO®), methemoglobin (SpMet®), and Pleth Variability Index (PVI®), in addition to SpO_2, pulse rate, and perfusion index (PI). Additional information about Masimo and its products may be found at www.masimo.com.

PREVENTION OF PERIOPERATIVE COMPLICATIONS

"IT TAKES A VILLAGE TO RAISE A CHILD"

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Introduction

Despite the increase in patients' baseline risk, according to the American Society of Anesthesiologists (ASA) score, perioperative mortality has declined over the last 50 years, particularly in developed countries (Bainbridge et al. 2012). Nevertheless, a recent large cohort study in 28 European countries demonstrated that the incidence of in-hospital mortality is relatively high at 4%, which is higher than previously expected (Pearse et al. 2012) as well as postoperative complications i.e. pulmonary and cardiovascular (Canet et al. 2010; Mazo et al. 2014). In an era when the prevalence of elderly and obese patients is likely to increase, perioperative complications in this group become the major concern due to their high risk. The development of postoperative complications is associated with long-term morbidity and financial loss. Financial loss includes not only long-term hospital stays but, also the expense of long-term follow-up, repeated admissions and chronic illness support. Multidisciplinary teams including surgeons, medical specialists, and anaesthesiologists could collaborate and plan for perioperative care leading to fewer medical errors and complications (Glance et al. 2014).

Prevention is the Target!

In the entire perioperative care pathway for minimising complications in high-risk patients, cardiovascular and pulmonary complications are the main factors affecting mortality. Cardiac risk factors have been widely recognised, and effective management to reduce perioperative cardiovascular morbidity and mortality has been generally implemented. In recent decades, postoperative pulmonary complications (PPCs) have become a major concern as they are associated with high mortality (Canet et al. 2010).

Unplanned ICU admission is associated with higher mortality rates. Several checklists and scores have been proposed to define the patients at risk for postoperative pulmonary complications (i.e. the postoperative pulmonary complications risk score (ARISCAT), the surgical lung injury prediction (SLIP) score and a score for prediction of postoperative respiratory complications (SPORC), which consist of simplified baseline factors and also objective factors that physicians can assess at the bedside. These scores can identify at-risk patients who require a multidisciplinary team approach and critical care resource allocation. The numbers of critical care beds in each country are heterogeneous, which may reflect the different outcomes. Nevertheless, the social benefit or harm of creating more intensive care unit beds is still debated. An increase in intensive care unit beds may increase harm in terms of unnecessary costs, iatrogenic complications, poor quality of care etc. On the other hand, shortages of intensive care unit beds may lead to delayed admission with potentially an increase in mortality. These link to the concept of a Starling curve for intensive care proposed by Wunsch et al (Wunsch. 2012). Changes in outcome may be related not only to intensive care unit beds but also to various factors i.e. the experience and training of the healthcare professionals as well as available resources at the ICU. Finally, emerging pulmonary risk factors, namely obstructive sleep apnoea, obesity hypoventilation syndrome and pulmonary hypertension, have been proposed. Concerning the increased incidence of PPCs in these groups, we may require further studies to improve the predictive score performance and monitoring technique in these groups (Weingarten et al. 2013).

Individualised Perioperative Monitoring and Care

Haemodynamic Optimisation

Recent meta-analysis has demonstrated that perioperative goal-directed therapy (GDT) reduced mortality in patients with extremely high risks of death (baseline mortality rate more than 20%). The mortality rate reduction was demonstrated in the studies using pulmonary artery catheter, fluid and inotropic drugs rather than fluids alone, and cardiac index and supranormal physiologic resuscitation target as a goal without further increase in cardiac complications i.e. arrhythmia, pulmonary oedema (Arulkumaran et al. 2014). Furthermore, the number of patients developing postoperative complications was reduced in the GDT cohort. These findings show that cardiac output and oxygen delivery targeting resuscitation affect perioperative outcome. Therefore perioperative GDT should be implemented in clinical practice at the right time (early), in the right patients and with the right protocol. However, further studies are warranted to show benefits of GDT in intermediate risk group patients (Cecconi et al. 2013).

Protective Ventilation and Respiratory Monitoring

The incidence of PPCs varies according to the definition, which can include pneumonia, respiratory infection, atelectasis, pleural effusion, pneumothorax, and bron-

chospasm, need of noninvasive ventilation or re-intubation. These complications are as common as cardiovascular events, and vary from 2.5% to 5% (de Abreu and Pelosi 2013). Recent experimental and clinical studies have shown, however, that protective mechanical ventilation might be relevant in non-acute respiratory distress syndrome (ARDS) lungs (Serpa Neto et al. 2012). Protective ventilation (low tidal volume of 6-7 ml/kg predicted body weight, high positive end-expiratory pressure [PEEP] level, between 6 to 10 cmH2O and recruitment manoeuvre) decreases the incidence of perioperative ARDS, pulmonary infection and atelectasis (Hemmes et al. 2013;Sutherasan et al. 2014).

Nevertheless, the recent large RCT, the PROtective Ventilation using HIgh versus LOw PEEP (PROVHILO), in intermediate and high risk abdominal surgery, has demonstrated that there was no difference in the first 5 days postoperative pulmonary complications between patients receiving high level of PEEP (12 cmH_2O) and recruitment manoeuvre and low level of PEEP (2 cmH_2O) without recruitment. Furthermore, patients in the higher PEEP group developed more frequent intraoperative hypotension and needed more vasoactive drugs compared with the lower PEEP group (The PROVE Network Investigators; for the Clinical Trial Network of the European Society of Anaesthesiology 2014), Therefore we suggest that an intraoperative protective ventilation strategy should include low tidal volume and low level of PEEP without recruitment manoeuvre.

The physicians use less invasive tools. In high risk postoperative abdominal surgery and obesity patients, beside pulse oximetry and end tidal CO_2 monitoring, chest wall elastance, transpulmonary pressure and intra-abdominal pressure should be measured. Lung ultrasound, a totally noninvasive tool, can be used to rapidly assess haemodynamic and pulmonary complications in the perioperative period (Cecconi et al. 2013; Sutherasan et al. 2014). In cardiothoracic and abdominal surgery, early postoperative physiotherapy can promote early mobilisation and respiratory muscle training, maintain adequate ventilation and prevention of PPCs (Makhabah et al. 2013). Noninvasive ventilation may prevent and treat postoperative atelectasis and lead to shorter duration of hospital stay in these subgroups, and can be used to treat postoperative respiratory failure (Jaber et al. 2010).

Biomarkers for Perioperative Management

Because postoperative adverse events are known to be the most important predictors of long-term mortality, it is necessary to improve preoperative identification of patients that may present greater risk of postoperative complications. Importantly, an improvement in such identification also allows more efficient use of healthcare resources. Traditionally, studies have been focused on identifying higher risk patients, those presenting potential cardiovascular complications (Barnett and Moonesinghe. 2011). However, beyond this important category, there are also other groups of patients with other potential complications, such as emesis, chronic pain, drug interactions or cognitive dysfunction, who may benefit from optimised perioperative protocols. In this context, biomarkers may represent a valuable tool, improving the prediction of short- and long-term outcomes.

Preoperative Biomarkers

The measurement of cardiac dysfunction plasma biomarkers such as B-type natriuretic peptide (BNP) or its precursor (N-terminal fragment (NT-proBNP)), has allowed a very significant improvement in cardiac failure management. BNP-guided therapy reduces all-cause mortality in patients with chronic heart failure (Porapakkham et al. 2010). Within non-cardiac surgery, meta-analyses have shown that elevated preoperative levels of BNP or NT-proBNP represent a powerful and independent predictor of cardiovascular events in the first 30 days after non-cardiac surgery(Karthikeyan et al. 2009). Despite this remarkable value of BNP, it is also important to take into account variability depending on the measurement assay, which may make it difficult to establish comparisons.

High sensitivity C reactive protein (hs-CRP) is a general biomarker of inflammation that offers important information regarding development and outcome of cardiovascular pathology. Beyond this, several studies have shown that higher preoperative hs-CRP levels are independently associated with perioperative complications both in cardiac and non-cardiac surgery (Ackland et al. 2007; Cappabianca et al. 2006). Nevertheless, it seems that when added to the Framingham Risk Score, CRP levels do not provide relevant additional information (Shah et al. 2009).

Postoperative Biomarkers

Several studies have demonstrated that elevated troponin levels are associated with mortality after major vascular surgery (Bursi et al. 2005). In a recent meta-analysis Levy et al. reported that increased postoperative troponin measurement is an strong independent predictor of mortality at one year, and therefore may help physicians to risk stratify patients after noncardiac surgery(Levy et al. 2011). In addition, levels of heart-type fatty acid binding protein (Muehlschlegel et al. 2010) and cardiac imaging strategies (Jerosch-Herold and Kwong. 2008) have also shown promising utility. Thromboelastography performed immediately after surgery has been associated with postoperative thrombotic complications, including myocardial infarction, in a diverse group of surgical patients (McCrath et al. 2005).

Acute kidney injury is also a very important determinant of the outcome of surgical patients. Besides creatinine or urea, other biomarkers may offer inter-

> **"Multidisciplinary teams …could collaborate and plan for perioperative care leading to fewer medical errors and complications"**

esting information about renal function in the early postoperative period. These include kidney injury molecule-1, cystatin C, neutrophil gelatinase-associated lipocalin, liver-type fatty acid binding protein as well as RIFLE score (Edwards et al. 2011;Waikar et al. 2008).

Neurological adverse events, such as stroke, delirium or cognitive dysfunction, are also frequent, and lead to prolonged intensive care unit stay and increased mortality. Markers of neurological damage such as S100B protein or neuronal specific enolase (NSE) have been studied in the postoperative period. Serum levels of S100B 24 hours after cardiac surgery have been useful to identify adverse neurologic outcomes (Georgiadis et al. 2000). Increased S100B in patients with a stroke following cardiac surgery correlated with the size of infarcted brain tissue and also showed an association with an increased risk of postoperative mortality (Jonsson et al. 2001). Furthermore, NSE and S100B concentrations 6 to 30 hours after cardiac surgery contributed significantly to a predictive model of the neuropsychological outcome (Herrmann et al. 2000). However, it should also be noticed that some studies have found conflicting results regarding the relationship between NSE levels and neurological outcome in several non-cardiac surgical procedures (Cata et al. 2011)

Summary

Haemodynamic and respiratory monitoring are essential in the perioperative period to minimise complications, particularly in high-risk patients, by early treatment and early allocated point-of-care. Studies investigating biomarkers require consistent characterisation of postoperative outcomes and adequate data collection of clinical phenotypes. A deeper knowledge of physiopathology will allow the identification of novel useful biomarkers that may help to stratify risk and improve patient's outcome by refining clinical management in the perioperative period. There is an African proverb, "It takes a village to raise a child", which means that the work of raising a child cannot be done alone; rather, an entire community must participate to some extent in the task. The collaboration between surgeons, anesthesiologists and medical specialists may lead to improved outcome in surgical patients. ■

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BLEEDING, COAGULOPATHY AND BLOOD PRODUCTS IN MAJOR TRAUMA

Transfusion of blood components in trauma can be lifesaving. Evidence for existing practice is being challenged, potentially with major blood supply implications, and novel therapies are under investigation.

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Introduction

The first human blood transfusion was performed in 1818 (Giangrande 2000), but not until the antigens distinguishing major blood groups were described in 1901 did transfusion become acceptably safe, at least for patients in the greatest need. Transfusion-transmitted infection is now a negligible hazard; other obvious adverse events (see Table 1 (Australian Red Cross Blood Service 2014)) are more common but largely amenable to treatment. Concern over subtler effects on immunity and inflammation is more recent, and emerged in the era of evidence-based medicine, leading to several large effectiveness trials, many of which are soon to report. A worldwide strategy known as "Patient Blood Management" (PBM) (2011) aims "to improve clinical outcomes by avoiding unnecessary exposure to blood components". Stopping bleeding is an obvious primary goal. However, seemingly in opposition to the blood-sparing goal of PBM, military and civilian trauma data show benefit from early blood (as opposed to non-blood fluid) resuscitation. Reconciling competing risks of early blood administration, blood avoidance, and more expensive blood substitutes and factor concentrates is now the subject of much research.

Stopping Bleeding

Haemorrhage is the most frequent potentially preventable cause of death, both in civilian trauma (Evans et al. 2010) and on the battlefield (Champion et al. 2003; Eastridge et al. 2012). Prehospital extremity tourniquets improve survival (Kragh Jr. et al. 2011); junctional (Klotz et al. 2014) and abdominal aortic (Taylor et al. 2013) tourniquets and endovascular balloon occlusion of the aorta (Brenner et al. 2013) show promise for more proximal wounds. Surgical management including preperitoneal packing, advanced imaging and an abbreviated "damage control" approach (Beckett and Tien 2013) all reduce bleeding and logically should reduce mortality.

Coagulopathy of Trauma

Trauma has an initially coagulopathic (Frith et al. 2010) and later procoagulant effect (Holley and Reade 2013), which suggests that early interventions to reduce coagulopathy may be helpful, but require careful longer-term evaluation. Coagulopathic trauma patients have modest falls in clotting factors, exacerbated by crystalloid fluid resuscitation, but a profound (>350%) increase in anticoagulant activated protein C (Cohen et al. 2013). Trauma-induced hypoperfusion and tissue damage also enhance fibrinolysis, causing an endogenous "acute traumatic coagulopathy" (ATC) (Frith et al. 2010) that may be quantitatively more important than clotting factor dilution, hypothermia or acidosis.

Massive Transfusion Protocols

The apparent reduction in major trauma mortality associated with higher ratios of plasma (Borgman et al. 2007) and platelets (Holcomb et al. 2008) to red cell resuscitation may be confounded by indication bias (Ho et al. 2012), but is nonetheless sufficiently intuitive to have been incorporated into national (National Blood Authority 2011) and international (Spahn et al. 2013) guidelines. Benefit may relate as much to preservation of endothelial integrity as to clotting factor concentrations (Jenkins et al. 2014). Up to 10% of military and 5% of civilian trauma patients require >10 units red cells transfused in 24 hours (Young et al. 2011), and protocolisation of at least the first few units results in greater efficiency (O'Keeffe et al. 2008). Point-of-care viscoelas-

tic coagulation testing is feasible, and although demonstrating patient outcome benefit in trauma may be impossible, is associated with reduced use of blood products (Görlinger et al. 2012).

Fresh Whole Blood

Whole blood, either warm / fresh or stored at 4°C for up to 21 days (Murdock et al. 2014), is a seemingly attractive alternative to component therapy. Over 6000 whole blood units were transfused in the wars in Iraq and Afghanistan, primarily due to supply issues (Spinella 2008). Theoretical risks include allergic reactions, transfusion-associated graft vs. host disease and transfusion-transmitted infection. A pilot 107-patient trial comparing leucodepleted cold-stored whole blood with component therapy suggested a lesser transfusion requirement in patients randomised to whole blood, (Cotton et al. 2013) with no more adverse effects. A definitive study has been proposed (Murdock et al. 2014).

Alternatives to Conventional Whole Blood and Blood Components

Lyophilised plasma was introduced during the second world war, but abandoned due to the transmission of hepatitis (Inaba 2011). Having now overcome this risk, the logistic advantage of a freeze- or spray-dried product stored at room temperature has excited considerable interest, particularly from the U.S. military. Currently used by the German, French and select U.S. units in Afghanistan (Jenkins et al. 2014), the U.S. military is funding a spray-dried solvent and detergent-treated type-specific pooled product (Resusix®, Entegrion, Research Triangle Park, NC, United States) that is yet to enter a phase III trial.

Conventional room temperature stored platelets have a shelf life of only five days, making their supply difficult outside large hospitals with predictably high demand. Various platelet analogues have been developed, including infusible platelet membranes, fibrinogen/thrombin microparticles, albumin microspheres coated with human fibrinogen (Modery-Pawlowski et al. 2013), and liposomes carrying fibrinogenγ-chains and adenosine diphosphate (ADP) (Nishikawa et al. 2012). None has yet reported phase III results. Platelets can also be cryopreserved in dimethylsulphoxide, extending their shelf life to two years. Although used in clinical practice by the Netherlands military since 2001, only now are two groups preparing for definitive phase III trials (Dumont et al. 2014.)

No artificial oxygen carrier has found universal acceptance. PolyHeme, a polymerised human haemoglobin, was assessed in a 714-patient trial that found no difference in mortality compared to red cell transfusion but more adverse events (Moore et al. 2009); the manufacturer subsequently became insolvent. Bovine cross-linked haemoglobin (Hemopure; HBOC-201) allowed 59.4% of 350 patients to avoid red cell transfusion, but produced more adverse events than in 338 controls (Jahr et al. 2008), and is currently registered for use only in South Africa. Polyethylene glycol-coupled haemoglobin is reported to be in early clinical trials, as are two perfluorocarbon-based emulsions. Glycerol-cryopreserved red blood cells have been used by U.S. and Dutch armed forces and recently introduced into Australian military practice, based on extensive clinical experience rather than comparative trials (Holley et al. 2013).

Pharmacological Treatment of Coagulopathy

Supra-physiologic doses of clotting factor concentrates raise the possibility that ATC may be actively treated. Factor VIIa reduced blood product use but had no

Table 1. Estimated Incidence of Tranfusion-Related Adverse Reactions (Australian Red Cross Blood Service 2014)

		Incidence (rate per total number of transfusions)
Haemolytic transfusion reaction due to ABO/Rh/other mismatch	Acute Fatal	1:76,000 1:1.8 million
Delayed haemolytic transfusion reaction		1:2,500-1:11,000
Febrile non-haemolytic transfusion reactions	Assuming universal leukocyte depletion	0.1%-1%
Allergic (IgE-mediated) reaction	Mild Severe (anaphylaxis)	1%-3% 1:20,000 – 1:50,000
Transfusion-associated acute lung injury	Male plasma confers less risk; the wide range reported reflects differing ability to supply all-male plasma.	1:1,200-1:190,000
Post-transfusion purpura		Rare
Transfusion-associated graft vs. host disease		Rare
Alloimmunisation	RBC antigens HLA anitgens	1:100 1:10
Transfusion-associated sepsis	Platelet transfusion Red cell transfusion	1:75,000 1:500,000
Transfusion-associated circulatory overload		<1%
Iron overload	Requiring chelation therapy Causing organ dysfunction if not treated	After 10-20 red cell units After 50-100 red cell units
Complications of massive transfusion	Hypothermia, coagulopathy, hypocalcaemia, kyperkalaemia	Variable (depends on quantity of product transfused, intercurrent treatments, and underlying patient condition)
Transmission of viral infection	Human immunodeficiency virus Hepatitis C Hepatitis B Human T-cell lymphoma virus Variant Creutzfeld-Jacob disease Malaria	<1:1,000,000 <1:1,000,000 1:538,000 <1:1,000,000 Theoretically possible <1:1,000,000

effect on mortality (Boffard et al. 2005; Hauser et al. 2010). European guidelines recommend factor VIIa be considered only if other measures have been unsuccessful. Fibrinogen is the first clotting factor to fall below critical levels in trauma. Fresh frozen plasma contains only 2g/L fibrinogen, whereas cryoprecipitate contains 8-16 g/L and fibrinogen concentrate 20g/L. Fibrinogen concentrate reduces the need for blood transfusion in cardiac surgery (Görlinger et al. 2011), but there are currently no trials and little observational evidence in trauma (Aubron et al. 2014). Lyophilised prothrombin complex concentrates (either 3-factor, with low factor VII, or 4-factor, with high factor VII) are well established for the reversal of vitamin K-dependent anticoagulants, and may have a role in trauma. Compared to plasma-based resuscitation, thromboelastograph-guided fibrinogen + prothrombin-complex concentrate reduced red cell and platelet requirements (Schöchl et al. 2011). Tranexamic acid blocks plasminogen activation, and so reduces fibrinolysis in addition to less well-characterised effects on inflammation. Tranexamic acid reduced mortality from 16% to 14.5% in the 20,211 patient CRASH2 trial (CRASH-2 trial collaborators 2010). Extrapolation of these results to prehospital care in the developed world is the subject of the PATCH-Trauma trial, currently underway (Mitra et al. 2014).

Effectiveness Trials Currently Underway

PROPPR (University of Texas Health Science Center, Houston) randomised approximately 680 patients expected to require a massive transfusion to plasma:platelets:PRBC 1:1:1 vs. 1:1:2. Recruitment was completed in December 2013. The Age of Blood Evaluation (ABLE) trial (Sainte-Justine Hospital Research Centre) randomised approximately 2500 patients requiring red cell transfusion to cells <8 days storage vs. standard care (2-42 days storage). The Red Cell Storage Duration study (RECESS) (New England Research Institutes) is randomising 1648 cardiac surgical patients requiring red cells to cells ≤ 10 days or ≥ 21 days, and the TRANSFUSE trial (Australian and New Zealand Intensive Care Research Centre) is randomising approximately 5000 ICU patients to standard-age red cells or the freshest available red cells in the hospital.

"Reconciling competing risks of early blood administration, blood avoidance, and more expensive blood substitutes and factor concentrates is now the subject of much research."

Management Issues – Cost-Effectiveness at a Population Level

Blood is a scarce resource. The World Health Organization recommends voluntary, non-remunerated blood donation (WHO Expert Group 2012), although there is some evidence that economic rewards do not increase risk of transfusion-transmitted infection (Lacetera et al. 2013), and are effective in increasing donor rates (Iajya et al. 2013). In Australia in 2011-2012, only 3.4% of red cell, 8.4% fresh frozen plasma, and 16.5% platelet units issued to hospitals and health providers were discarded (National Blood Authority 2014). Any change to recommendations for individual patients must therefore take account of the effect on the global blood supply. For example, if ICU patients derive benefit from receiving the freshest possible red cells, what effect will this have on other trauma patients? If 1:1:1 is optimal in massive transfusion, what are the implications for plasma supply to other patients? These questions will almost certainly confront blood service managers in the near future.

Patient Blood Management (PBM)

PBM aims to reduce "unnecessary" exposure to blood components. An audit of ten Australian hospitals found 35% of red cell transfusion episodes included inappropriate units (defined by similar criteria to those of PBM) (Rubin et al. 2000). PBM is a rational response to both the new "evidence-based" paradigm in blood transfusion, and a means of conserving the blood supply. Adopting PBM must itself be evaluated, ideally through prospective registries such as the massive transfusion registry of the Australian Blood Centre of Research Excellence (http://www.anzicrc.monash.org/blood-cre.html).

Conclusion

Renewed interest in blood product resuscitation for major trauma has occurred in the era of evidence-based medicine. Existing therapies are currently the subject of effectiveness trials that will impact both individual patient management and that of the blood supply. While existing blood products became established in practice largely on the basis of anecdote, theory, and absence of immediate adverse effects, the evidence required of new or alternative therapies is comparable to that of pharmaceuticals. Regulators must balance caution with innovation in what has, until recently, been an evidence-free field. ■

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ADEQUATE DIALYSIS IN THE ICU
A MULTIDIMENSIONAL ASPECT

Prescription and delivery of an adequate treatment is a fundamental issue in a critically ill patient but especially when he or she requires continuous renal replacement therapy. This short review will detail basic concepts related to the dialytic dose and current evidence available on this topic. The paper further expands the concept of adequacy leading to other important dimensions of treatment adequacy.

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Efficiency, Intensity, Efficacy

Acute kidney injury (AKI) is frequently observed in critically ill patients, and approximately 6% of the ICU population receives renal replacement therapy (Uchino et al. 2005). Continuous renal replacement therapies (CRRT) represent an extracorporeal dialysis modality particularly suitable for haemodynamically unstable patients who require fluid and solute control (Davenport et al. 1993; Uchino et al. 2001; Swartz et al. 1999). This feature is one of the reasons why many physicians prefer CRRT in intensive care patients rather than intermittent haemodialysis (Uchino et al. 2007). Several factors may affect the efficacy and safety of these procedures (Uchino et al. 2007), and particular attention is usually paid to treatment adequacy, which may allow reproduction, as close as possible, of the function of the native kidney. In this context, CRRT technique and treatment parameters (flows and clearances) are often protocoled, and the adequacy has been generally identified with the concept of dose (quantity of a marker molecule removed over time or as a fraction of the blood flow).

Dialytic dose may be represented in many ways: efficiency (or clearance) of the treatment is the amount of blood cleared by the system over a given period of time (Ricci et al. 2006). The concept of clearance needs to be referred to a particular solute, and it does not represent an actual mass removal, but rather its value normalised for the solute serum (or plasma) concentration. Moreover, considering that CRRT is usually performed over several days or weeks, it is essential to provide information about the total time during which the treatment clearance is maintained. The intensity of treatment is thus expressed as the product of the clearance (instantaneous) and the effective time of treatment (Ricci et al. 2006). Prescribed and effective treatment time may differ significantly. If one calculates the downtime (the amount of time in which the treatment is interrupted), significant difference can be found between the prescribed and the actually delivered doses. Finally, considering the pool of solute (related to volume of distribution) that needs to be cleared, it is possible to express the efficacy of the treatment as the ratio between Intensity (in litres) and the volume of distribution of the marker solute (in litres) (Ricci et al. 2006). The result is a dimensionless number defined as Kt/V (Clearance x time / volume of distribution).

In chronic kidney disease (CKD) patients treated with haemodialysis, efficiency, intensity and efficacy are routinely measured because they correlate with long term outcome (Ronco et al. 1996). In AKI patients treated with CRRT in the ICU, these variables may be grossly estimated considering the effluent flow rate set in the CRRT machine (Uchino et al. 2007) (or directly measured) and then by indexing it over the patient body weight (i.e. if a 60kg patient is treated with 1200 ml/h of isovolaemic post-dilution haemofiltration, the treatment dose may be indicated as 20 ml/kg/h). As for every simplification, with this method a relatively broad level of error should be accepted, especially when continuous pre-dilution haemofiltration or continuous haemodialysis are delivered. Furthermore, the estimation does not take into consideration the progressive fall of membrane performance during the length of the session (especially after the first 24 hours). Nevertheless, the ease of this calculation may be very useful in real clinical life (Ricci et al. 2005).

How to Pick the Dose

Several efforts have been made in the literature to define the most adequate dose: the idea is that CRRT delivery may imply a dose-dependent range, where the treatment efficiency correlates with outcomes, and a dose-independent range, in which further improvements will not result in more benefits for these patients. Consequently, during the last decade, several attempts have been made to confirm the first dose proposal (35 ml/kg/h) that showed a direct correlation between CRRT efficiency and patients' outcome (Ronco et al. 2000). However, the RENAL (RENAL Replacement Therapy Study Investigators et al. 2009) and the ATN (VA/NIH Acute Renal Failure Trial Network et al. 2008) studies seemed to definitely confute this evidence. These two large multicentre, randomised controlled trials did not show an improved outcome with a "more intensive dose" (40 and 35 ml/kg/hr respectively) compared to a "less intensive dose" (25 and 20 ml/kg/hr respectively) (Ricci and Ronco 2011). Based on these findings, the current KDIGO guidelines recommend delivering an effluent volume of 20–25 ml/kg/hr for CRRT in patients with AKI (Kidney Disease: Improving Global Outcomes 2012).

In addition, by comparing two multicentre CRRT databases, Uchino et al. found that treating patients with AKI with low-dose CRRT was not associated with worse short-term outcome compared to patients treated with what is

currently considered the standard dose (Uchino et al. 2013). In particular, comparing patients from The Beginning and Ending Supportive Therapy (BEST) study (Uchino et al. 2005) and from the Japanese Society for Physicians and Trainees in Intensive Care (JSEPTIC) Clinical Trial Group (Kawarazaki et al. 2013), the author observed no differences between groups of patients treated with doses of 14.3 ml/kg/hr and 20.4 ml/kg/hr.

Finally, considering that high-dose CRRT could lead to electrolyte disorders, removal of nutrients and drugs (e.g. antibiotics) and high costs (Rimmelé and Kellum 2011), but at the same time low-dose may expose patients to under-treatment thus worsening outcome, seeking the range of adequate treatment dose is a crucial issue. Nowadays, it is considered as clinically acceptable an actually delivered dose (without downtime) between 20 and 35 ml/kg/hr (Uchino et al. 2013). In particular a dialytic dose under 20 ml/kg/hr and over 35ml/kg/hr may be definitely identified as the dose-dependent range. On the other hand, the doses between these two limits can be considered as practice-dependent, and variables such as timing, patient characteristics, comorbidities or concomitant supportive pharmacological therapies may have a significant role for patients' outcome.

How to Customise the Dose

The innovations in diagnosis, classification and prevention of AKI and the development of fourth generation CRRT machines, specifically designed for critically ill patients with particular attention to safety features and accuracy, have modified the idea that dialysis in these patients is indicated only after the development of anuria. The redefinition of AKI treatment, different than mere renal replacement therapy, allows modulation of the timing, indication and prescription for personalised renal support therapy. In this context, it could be speculated that conventional protocoled treatments (that in most cases might be seen as "rescue therapies") are substituted by proactive therapy, which can be modulated according to the different phases of patient clinical condition observed during the ICU stay (Ricci et al. 2011).

In these terms, dose, filter membrane characteristics, anticoagulation and fluid solution should be utilised to tailor the treatment to patients' specific needs.

One of the key issues of the modern concept of renal support therapy is the clinical target: deriving from nephrology considerations, urea is the main solute, which has been referred as the biomarker indicating how efficiently solutes are removed. However, urea is not the only solute accumulated during kidney injury and its kinetics of removal and its volume of distribution differ from the other uraemic toxins (Ricci et al. 2006). Moreover, considering urea as a target solute may lack clinical usefulness. Unlike patients with chronic kidney disease (CKD), uraemic symptoms are rarely observed in the ICU, and usually do not affect clinical decision-making regarding CRRT in these patients (Ricci and Ronco 2012). Other target solutes, different from urea, should be considered in ICU patients. In particular, CRRT should be directed at specific targets during specific clinical conditions (e.g. myoglobin in a patient with compartment syndrome, interleukins during septic episodes, novel biomarkers in case of early AKI, fluid balance in case of fluid overload). This concept would also redefine the concept of adequacy itself, including not only the amount of dialysis to provide but also the exact circuits, filters, machines and timing.

Fluid overload probably deserves a dedicated paragraph: it is currently considered one of the most important indications for CRRT in the ICU. Although not easy to assess and currently not included in any standardised definition, the fluid removal (net ultrafiltration) obtainable during CRRT can be personalised to patient clinical condition and should be carefully targeted. For example, in a post hoc analysis of the RENAL trial the authors showed that duration of mechanical ventilation, length of stay and survival was significantly improved if negative fluid balance was reached before 48 hours after CRRT start (RENAL Replacement Therapy Study Investigators et al. 2012). Much effort will have to be paid in the near future in the field of monitoring fluid administration, fluid loading and fluid downloading.

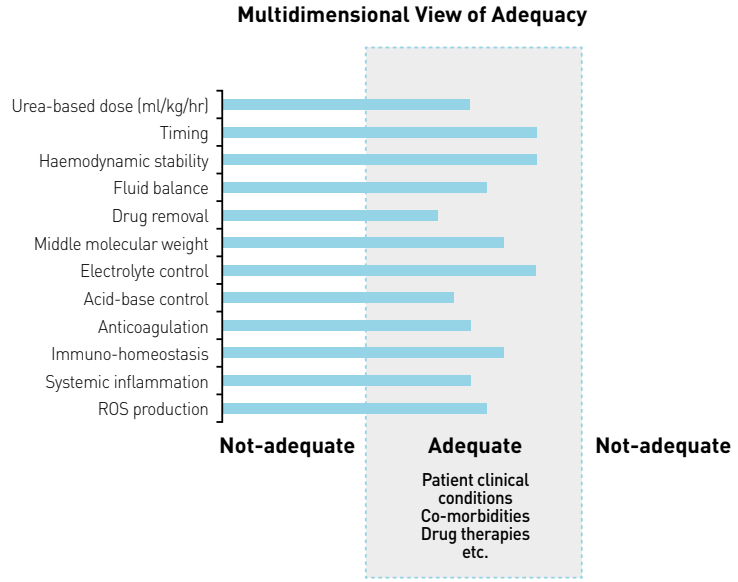
Furthermore, although operatively simple and, by analogy with CKD patients, potentially related to hard outcomes, a target-based approach might be too simplistic and "mono-dimensional". Dimensions of adequacy other than dose, e.g. body fluid composition modification, electrolyte, acid-base or tonicity control, should be evaluated in critically ill patients (Ricci et al. 2006) (see Figure 1).

Anticoagulation (and filter patency) is another

fundamental issue strictly related to dialysis delivery and to the personalised prescription of an adequate CRRT treatment. Systemic and regional anticoagulation, as well as heparin grafting membranes, are potentially able to reduce the filter clotting and consequently the membrane fouling. Analysing data from the PICARD study, Claure-del Granado et al. evaluated the association of anticoagulation strategy used on solute clearance efficacy and circuit longevity (Claure-del Granado et al. 2014). In particular the authors showed that, if compared to heparin or no anticoagulation, the use of regional citrate for anticoagulation in CRRT significantly prolonged filter life and increased its efficacy in term of delivered dose (Claure-del Granado et al. 2014). Despite the most recent guidelines suggesting use of regional citrate anticoagulation in patients without contraindications (Kidney Disease: Improving Global Outcomes 2012), systemic unfractioned heparin remains the most used anticoagulation during CRRT. The anticoagulation choice could also be referred to the therapeutic target to be obtained for that specific patient, and depends on his or her clinical condition, vascular access, kind of membrane and target solutes, which have to be removed. In a prospective study on septic patients, De Vriese et al. clearly demonstrated that membrane dysfunction affected cytokine clearance during CRRT treatment (De Vriese et al. 1999). Unfortunately, this predictable mechanism is not simply quantifiable in clinical practice. When the membrane fouling occurs and clearance of urea (a 60-dalton non protein-bound molecule) falls by 20%, the clearance of larger solutes may have already been impaired in the CRRT circuit life span (Pasko et al. 2011). In this context, if middle molecular weight molecules are the solute target to be removed, accurate anticoagulation should be performed also to ensure that an adequate sieving coefficient for these molecules is maintained for a long period of time.

> **"Dialytic prescription is a recipe where different ingredients have to be adequately balanced from patient to patient"**

Figure 1. Several Patient Characteristic Have to be Evaluated (in this figure dimensionless graphic representation is offered) in order to personalize the CRRT in the ICU and the treatment characteristics consequently modelled to be adequate for the actual patient necessities



Attention has to be paid to the dialysate and replacement solutions used during CRRT. An adequate control of electrolyte and acid-base disturbances is usually obtained through a personalised choice of modality of depuration and fluid solutions utilised. The specific ion composition in the dialysate or in the replacement solutions allows, for example, a more accurate control of hyperkalaemia or phosphate reintegration during CRRT. In particular, hypophosphataemia has been reported in up to 80% of cases when standard CRRT solutions are used (Demirjian et al. 2011; VA/NIH Acute Renal Failure Trial Network et al. 2008; RENAL Replacement Therapy Study Investigators et al. 2009). The adoption of phosphate-containing CRRT solutions could be helpful to reduce the incidence of RRT-related phosphate depletion, and to minimise the requirement of parenteral supplementation (Broman et al. 2011).

The different buffers and their balance mass evaluation may allow restoration of acid-base homeostasis in critically ill patients when the underlying cause is going to be resolved. In these patients, acidosis is usually due to increased unmeasured anions and hyperlactataemia: CRRT is able to correct these conditions affecting the patient's strong ion gap, phosphate and chloride concentrations and, in particular in persistent hypoalbuminaemic patients, may further lead to metabolic alkalosis (Naka and Bellomo 2004). The nature and extent of acid–base changes are related to the treatment intensity and to the 'buffer' content of the replacement fluid/dialysate, with different effects depending on whether lactate, acetate or bicarbonate is used (Naka and Bellomo 2004). Moreover, during regional anticoagulation performed with citrate, the amount of citrate returning to the patient and metabolised by the liver and the skeletal muscle in the Krebs cycle results in bicarbonate production providing buffer supply to the patient. The amount of citrate administered to the patient has to be evaluated for the buffers mass balance (Morabito et al. 2013).

In conclusion, a specific treatment that could be defined "adequate" for all patients in all conditions does not exist but, like mechanical ventilation, CRRT should be continuously tailored to patients' characteristics and their actual clinical needs. Dialytic prescription is a recipe where different ingredients have to be adequately balanced from patient to patient and it is not to be seen as an index derived from the rigid application of simplified recommendations. ■

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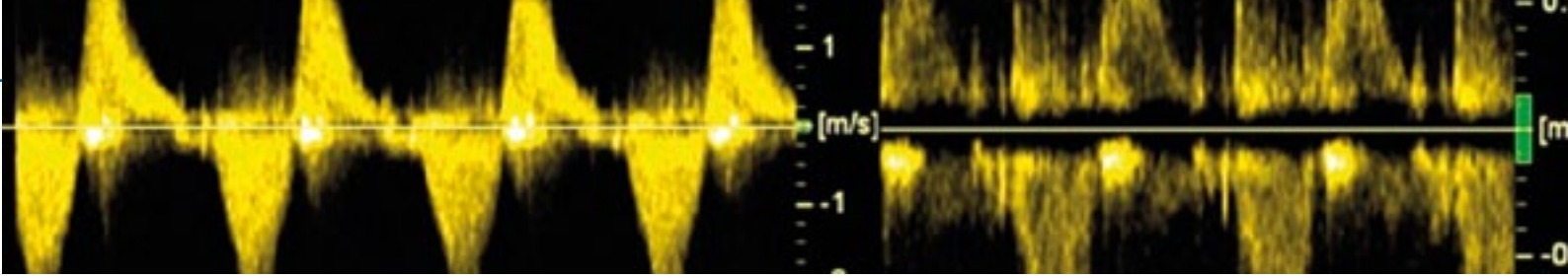

International Course

Echocardiography for Hemodynamic Monitoring 2014

with videotransmissions of live cases from the ICU

Brussels, November 18-20, 2014

Course directors
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Michel Slama (Amiens, France)
Antoine Vieillard-Baron (Boulogne-Billancourt, France)

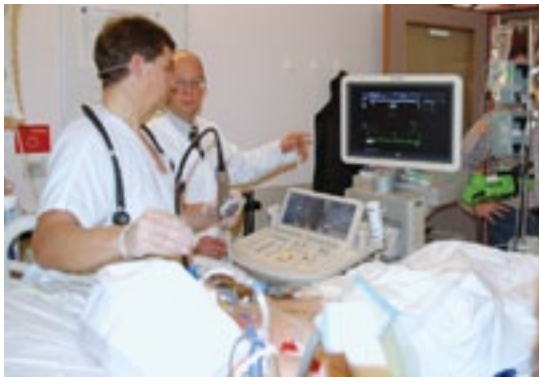
Special guest speakers:
Paul Mayo (New York, USA)
Anthony McLean (Sydney, Australia)

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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ROLE OF INTENSIVISTS
IN EMERGENCY MASS CRITICAL CARE

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Emergency Mass Critical Care (EMCC) is limited, essential critical care during disasters when critical care demand surpasses traditional resources. The intensivist must play an integral EMCC planning and response role.

Introduction

Disasters and pandemics can result in large numbers of critically ill patients that can overwhelm our current capacity to deliver critical care services. Such imbalance between critical care demand and resources can result in lives lost, as evidenced during disasters such as Hurricane Katrina and the Japanese Tohoku earthquake and tsunami. However, loss of lives can be prevented or at least decreased with adequate preparation, which includes coordination of services and resource allocation involving critical care capacity and readiness at the regional, hospital, unit, and individual provider levels. This preparation is best achieved using the principles of crisis standards of care and a surge capacity continuum as outlined for Emergency Mass Critical Care (EMCC) response.

Emergency Mass Critical Care Overview

EMCC delivery can improve patient outcomes and lives saved by conserving, optimising and better matching critical care resources to critical care demand. EMCC was well described by the Task Force for Mass Critical Care (Devereaux et al. 2008a). It encompasses a system-wide approach of matching critical care resources to critical care demand during disasters, utilising the principles of crisis standards of care and a surge capacity continuum. Unfortunately, critical care providers still receive little training in disaster medicine and response and are often uninvolved in hospital disaster preparedness efforts. This current lack of EMCC awareness, training, and preparation by critical care providers became clearly evident during the Hurricane Sandy intensive care unit (ICU) evacuations (Powell et al. 2012).

The goal of this review is to educate the ICU provider about the principal concepts of EMCC so they may be better prepared and organised to provide care and save lives during future disasters. We also hope to provide the ICU provider with a new perspective about their integral role in disaster response so that they may take an active role in preparing their own hospital and broader community for delivery of EMCC. Delivery of critical care during a disaster will only be successful if ICU providers work in partnership with the larger disaster preparedness system. Given the very specialised nature of critical care, intensivists have a professional obligation to participate at all levels of EMCC decision-making.

Crisis Standards of Care

Critical care resources, including ICU bed spaces, critical care staff, and critical care supplies, can limit our ability as critical care providers to improve patient outcomes, even during routine surge situations. During disasters, critical care demand can overwhelm standard resource levels, and definitions of critical care space, staff and supplies need to be modified. The United States Institute of Medicine (IOM) issued guidance for healthcare facilities and providers entitled Crisis Standards of Care that provides a systems framework for catastrophic disaster response (IOM 2012). This framework, with minor variations in names depending on country nomenclature, provides the broad principles on which any EMCC response system can be designed. Within this report the IOM described the Foundation of Crisis Standards of Care as an edifice with five pillars: Hospital Care, Public Health, Out-of-Hospital Care, Emergency Medical Services (EMS) and Emergency Management & Public Safety. Hospital care is just one pillar that must work in conjunction with these other four pillars to execute an effective mass crisis response. The IOM also recommended utilising standard nomenclature to describe the three categories of

surge capacity: conventional, contingency and crisis, as described below (Hick et al. 2009).

Surge Capacity Continuum

Conventional, contingency and crisis capacities exist along a surge capacity continuum during critical care disasters, both when incident demand and/or resource imbalance increases and patient morbidity/mortality risk increases as well as during the recovery phase.

Conventional capacity denotes usual care standards (implemented in major mass casualty incidents and representing care as usually provided at that institution.)

Contingency capacity denotes different but functionally equivalent care standards (using adaptations to medical care spaces, staffing constraints and supply shortages without significant impact on delivered medical care).

Crisis capacity denotes true crisis standards of care (implemented only in catastrophic situations with a significant impact on standard of care.)

One can conceptualise an initial step in expanding critical care space and capacity by providing critical care in lesser acute units (Rubinson et al. 2008). Progressive expansion of critical care in sustained crisis conditions such as pandemics (Stiff et al. 2011) includes critical care encompassing a much larger proportion of hospital care with further expansion in other areas of the hospital.

Transition from conventional to contingency capacity should be triggered when a potential for crisis standards of care is identified. This often happens in resource-limited areas on a regular basis and in others during self-limited surges in patients. Transition from contingency to crisis capacity should only be triggered by a true initiation of crisis standards of care at the hospital and/or regional level and usually after discussions involving senior critical care clinicians, administrators and regional disaster coordinators. Thus this transition to crisis capacity should only occur via official hospital and/or regional policy, and these principles cannot be cavalierly applied by individual providers. However, it is paramount that the critical care provider understands these principles and their role in both identifying critical care demand/resource imbalances and responding under altered care environments.

Paediatric Surge Capacity Inadequacy

Special attention should be paid to the inadequate paediatric critical care resources that currently exist for disasters (Kissoon and Task Force for Pediatric Emergency Mass Critical Care 2011; Stamell et al. 2009). Children comprise approximately 25% of the general population, and are especially vulnerable during disasters for a variety of anatomic and physiologic reasons. There are other compelling reasons to include issues related to children in all planning exercises, such as the fact that 80% of disaster victims including children will transport themselves (or be transported by their caregivers) to the nearest medical facility (Gausche-Hill 2009). In addition, most paediatric hospital care is regularly delivered at relatively few large regional paediatric centres (Halpern and Pastores 2010), and paediatric hospitals can be inaccessible geographically and/or have far too few beds during times of disaster to meet the needs of critically ill children (Odetola et al. 2005). This disparity between paediatric and adult access to critical care resources can be glaringly out of proportion should both populations be equally affected. Paediatric populations are often disproportionately affected during pandemics, as seen during the H1N1 influenza pandemic.

Thus, one important area of surge capacity that all adult intensivists must consider is the potential need to expand their surge capacity to include paediatric care. Adult providers who do not routinely provide paediatric critical care must consider the staff (those with an interest or training), supplies, tools and education that could enable EMCC delivery to children. One simple tool that enables many EMS and emergency department providers to provide paediatric critical care is length-based colour-coded tape. Length-based colour-coordinated tapes improve the provision of properly sized critical care equipment and medications (Agarwal et al. 2005). Coordination with regional paediatric centres to share protocols and staff and to obtain just-in-time consultation is also advisable.

Ethics During Disasters

The descriptions of crisis capacity may include: 1) operating in a damaged and/or unsafe facility; 2) having unavailable critical care staff for the number of patients; and/or 3) lacking basic critical care supplies such as mechanical ventilators. Functioning as a critical care provider under such extreme conditions can be both stressful and ethically complicated. Altered standards of care may require critical care providers to operate under different ethical principles compared to everyday practice, such as optimising population health over individual patient health. Many ethical issues encountered during disasters centre around the issue of allocation of limited life-saving resources. During Hurricane Sandy, the issue of mechanical ventilator allocation arose when power was threatened, and intensivists were put into the situation of attempting to determine how patients should be prioritised (Uppal et al. 2013).

Intensivists typically provide care on a first-come, first-served basis, and only perform critical care triage under rare circumstances, such as in the instance of limited extracorporeal membrane oxygenation (ECMO) circuits. Thus intensivists in

"Delivery of critical care during a disaster will only be successful if ICU providers work in partnership with the larger disaster preparedness system"

the developing world receive little to no education about how to ethically conduct triage of limited life-saving resources. A basic principle of ethically sound triage is that the degree of rationing is proportional to the actual or anticipated resource deficiency (Barnett et al. 2009). It is also of paramount importance that hospitals within a given geographical region conduct consistent and coordinated triage between and among adult and paediatric critical care communities to ensure equitable allocation of resources among a population (Devereaux et al. 2008b). Intensivists must therefore be actively involved at all levels of critical care allocation decisions, from creation of the regional, national and international critical care triage policies, to adoption and testing of these policies at the hospital level, and practising as a member of a critical care triage team.

Communication and Evacuation

ICU providers should also consider communication and evacuation issues in regards to the special needs of their critical care patients. Communication has been extremely problematic for ICUs during disasters, as phone lines and computers can malfunction, and situational awareness is often poor. Redundant communication systems and tools must be developed for ICUs for communicating within each unit, with hospital incident command and potentially with outside hospitals. Specific to ICU evacuation, both paper and electronic evacuation forms should be available given the potential for no power, as seen during Hurricane Sandy. Perhaps most importantly, a system for regional communication in the event of a large scale disaster and/or evacuation must include critical care input, as inpatient critical care patients often require very specialised transport, staff or equipment needs that may not be appreciated by non-critical care providers (Schultz et al. 2003; Iwashyna et al. 2009; Fuzak et al. 2010; Verni 2012).

Where to Start?

After ensuring their own personal emergency preparedness plan at home, one good place for every intensivist to start is to ensure the preparedness of their own unit. We recommend referring to a checklist titled Concise disaster planning checklist for intensive care unit clinicians (Daugherty and Rubinson 2011.)

Although preparing one's unit is important for delivering EMCC, preparation is most dependent on collaborative work between critical care providers, hospital disaster planners and regional disaster planning groups, sometimes referred to as "Healthcare Coalitions." Thus, intensivists must become educated in disaster medicine, participate in hospital disaster planning and drills, and play active roles with regional disaster planning groups to help create disaster plans that support the unique critical care needs of patients in their geographical region.

Conclusion

In this manuscript we have reviewed the fundamental concepts related to EMCC as a primer for further education. The ICU provider must become better educated about Emergency Mass Critical Care (EMCC) so they may be better prepared and organised to save lives during future disasters. Intensivists also have a professional obligation to play an integral role along the continuum of EMCC planning and delivery. ■

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EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

INTERVIEW WITH PRESIDENT-ELECT PROFESSOR DANIEL DE BACKER

Professor Daniel De Backer is President-Elect of the European Society of Intensive Care Medicine, and takes up his role as President in October 2014. He is Professor in the Intensive Care Department at Erasme University Hospital in Brussels, Belgium.

What Motivated you to Stand for the ESICM Presidency?

In my daily practice, I combine bedside clinical care, research and teaching, all these being the points of interest of ESICM. In the past I have been deeply involved in ESICM and other scientific societies as I consider that scientific societies are the most suitable bodies to promote science and good clinical practice to young as well as older colleagues. As a Belgian, living in a small country open to the entire world, I rapidly understood that we would think better at the European level rather than at our limited regional/national level. In my past roles in the society, initially as National Representative to the ESICM Council, and later as Section Chair and Chair of the Research Committee, I realised what ESICM can bring to its members: opportunities to conduct high level science, promote collaborative projects, provide education and training by the best trainers in Europe, facilitate recognition of a specialty, promote awareness of intensive care medicine among the lay public and decision-making bodies. Accordingly, I decided to apply as candidate for President-Elect, hoping that my experience in previous positions in the Society and other scientific societies, and my position as a renowned researcher and teacher would be helpful for ESICM.

What Are your Goals as ESICM President?

1. **Encourage research**, especially for young investigators. For decades, ESICM members have conducted high quality research. ESICM already offers various awards, and these should be multiplied. ESICM should facilitate mobility of investigators and collaboration of research groups among its membership.

2. Foster collaborative research (through ESICM Trials group). This trial group is now conducting large scale observational trials. ESICM should encourage this group to conduct large scale randomised interventional trials. Many of our interventions and practices are not supported by strong evidence. Investigator-driven research should grow and be supported by ESICM with the help of regulatory agencies (EC).

3. Promote recognition of intensive care. Intensive care often lacks recognition by national and international (including EC) agencies. ESICM should also facilitate public awareness of intensive care. This would need lobbying and promotional campaigns.

4. Facilitate teaching. In addition to existing facilities (EDIC course, new e-learning platform), ESICM should further extend the use of modern technologies. With the current economic crisis, many members from countries subject to economic restrictions will have more difficult access to existing facilities. ESICM should develop new modes of teaching (using online facilities). In this domain, web-based ICU rounds can be developed, with online discussions of cases from various ICUs in Europe.

5. Develop a European diploma for advanced critical care echocardiography. Echocardiography is now part of our daily practice in the ICU. If most physicians now master basic echocardiography, which is now part of the critical care curriculum, advanced echocardiography is still restricted to a minority of experts, even though it can really be used (and is recognised) as a powerful monitoring technique. Recently, I was part of a group of experts representing several scientific societies around the globe, who defined the curriculum for training in advanced critical care echocardiography. In the next few years I would like to settle the basis for a European diploma in advanced critical care echocardiography.

6. ESICM should be a meeting point for clinicians, with creation of a clinician centre, online discussion of selected cases by renowned ESICM experts, and other related initiatives.

What Are You Most Looking Forward to at the ESICM Congress in Barcelona?

Once again the annual ESICM congress promises to be a great event, gathering more than 6000 attendees from everywhere around the globe. In addition to the many state-of-the-art meetings, the presentation of several thousand original abstracts covering most fields of experimental and clinical critical care medicine is one of the most important attractions of

the congress. Young as well as established scientists will present their brand new results and present to the interested and critical minds of colleagues. I remember this important aspect when, as a young investigator, I was presenting my own data to the ESICM congress. In addition to the natural pride resulting from presentation of my data in front of renowned scientists, the comments raised were often very useful in writing my papers. Finally, Barcelona will be for meeting colleagues, otherwise often very busy, in a friendly atmosphere.

What Do You See as the Major Challenges for Intensive Care in Europe? How Do We Find Solutions?

Collaborative research in Europe: We have a long and glorious history of research performed by individual groups or by groups of friends. In more recent years, national networks have arisen, but multinational collaborative research in Europe is still lacking. However, this is absolutely mandatory if we wish to address questions requiring large sample sizes, in observational as well as in interventional trials. In addition, it would also address the issue of external validity of the results, as investigating patients from all parts of Europe would ensure that the results apply to all these.

Mobility across borders: EU recognises the right for any worker within the EU to move and work in another EU country. This is also true for medical doctors and specialists. Unfortunately, the intensive care specialty is not recognised as such (either as primary or secondary) by European institutions. As, in addition, training in intensive care varies widely across Europe, certification acquired in one country is often not recognised in another one. ESICM has long worked on this topic, establishing first the picture of how training is performed in Europe and defining core competencies in critical care though the CoBaTrice program, through the European Diploma in Intensive Care, and working with European bodies to achieve recognition of intensive care competency.

> *"ESICM should be a meeting point for clinicians"*

Recognition and awareness of intensive care medicine. Lobbying and having ICU survivors proudly testifying the usefulness of ICU.

You Have Wide-Ranging Research Interests. Could You Tell Us About Your Current Research in One of These Areas?

My main topic of interest for research is circulatory failure, from haemodynamic monitoring, including regional circulations and the microcirculation, to drug and mechanical therapies, including organ support.

These last 10-15 years I have been extensively focused on the microcirculation, being one of the first to describe these microcirculatory alterations in critically ill patients, demonstrating at the bedside the concept of microcirculatory shunt, and evaluating the effects of several potential interventions.

You are Principal Investigator of the Fluid Challenges in Intensive Care (FENICE) Observational Trial. Can You Tell Us More About This?

This multinational multicentre observational trial was conducted under the umbrella of the ESICM Trials group, for which it was its first large scale trial. This trial included more than two thousand patients in 311 centres in 46 countries. We addressed a very simple but important question: how do physicians conduct fluid challenge at the bedside? In particular, we were interested in defining what are the indications for fluid boluses, how these are indicated and monitored, what are the effects of fluids and whether these were tolerated. We are currently writing the manuscript and hope to publish the results soon.

What Do You Think Should Be Priorities For Intensive Care Research?

No great novelty here, we should continue to try to better understand the pathophysiology of the various diseases that contribute to significant morbidity and mortality in the critically ill patient, and develop new therapeutic strategies.

Focusing on sepsis, one of my main fields of interest, we should really advance on the different stages: improve recognition, better antibiotic strategies (especially given the high resistance profiles encountered), better initial management (including resuscitation process), and optimise organ support. A crucial point is to understand what makes a patient recover from sepsis. We are often confounded with cases of patients with controlled source of sepsis but protracted organ dysfunction. Some of these patients suddenly improve, some worsen and die. We often fail to understand what are the factors contributing to the improvement or worsening, and better understanding these mechanisms may help to develop new therapies that could help to increase the number of survivors.

This Interview Will Be Published In Our Autumn Issue With a Cover Story on Communication. What Do You See as the Main Issues with Communication in the ICU?

Communication in the ICU is essential. Communication within the ICU team has markedly improved, but progress can still be made. Communication with patients and relatives has been a topic of intense research and major improvements have been observed. Opening the ICU to relatives is probably the next frontier. Data support opening our ICUs to relatives, but implementation in practice is often complicated. I recently signed an editorial with Mitchell Levy (Levy and De Backer 2013) on the advantages of an ICU open to relatives 24/24. We now welcome presence of relatives even during CPR (Jabre et al. 2013).

Finally, communication with the lay public is minimal and contributes to a lack of recognition. Who knows exactly what an ICU is if not confronted with it personally? We daily save thousands of lives throughout the world but do not receive the credit deserved for it. ■

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MicroVision Medical launches instant microcirculation analysis at the bedside:

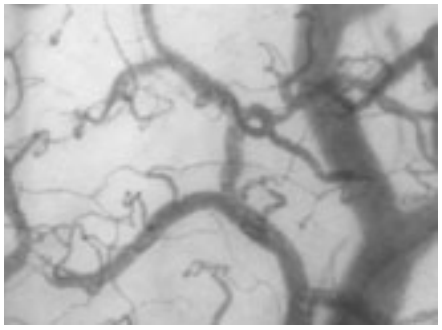
A new tool to quantify the microcirculatory effects of (fluid) resuscitation

Ever since the introduction of microcirculatory monitoring at the bedside, physicians and clinical investigators have had one wish: to instantly have an analysis of the microcirculation at the bedside.(1)

The fourth generation of MicroVision Medical's Automated Vascular Analysis (AVA) application makes this wish a reality. In less than 5 seconds after capturing 15 frames, the user will be presented results that include density and flow.

User friendly and instant application:
The step by step software will guide the user to obtain high quality images by giving real-time feedback on light intensity, focus and stability. This allows for capturing of high quality patient data that is analyzed reliably.

This latest version AVA is built from the ground up with user-friendliness in mind. The users' only decision is on which site in the patient to perform the measurement. The algorithms have been completely rewritten allowing for more detailed analysis and improved vessel detection. This increases the level of sensitivity for microvascular derangements.



Sublingual microcirculation visualised by the MicroScan

All key microcirculation parameters with one press of the button
The measurements will present the user with a list of parameters which include the De Backer score as defined by Prof. De Backer in his paper "How to evaluate the microcirculation: report of a round table conference"(2):

- Total vascular density
- Small vessel density
- Proportion of perfused vessels (all)
- Proportion of perfused small vessels (PPV)
- Perfused vessel density (all)
- Perfused small vessel density (PVD)

The density measurements will be both in number of crossings on a grid of six lines as well all based on (a proportion of) vessel length as described by Prof. De Backer.
We expect the new AVA 4.0 package to help ICU physicians to deepen their understanding of the importance of the microcirculation during resuscitation of septic patients and in time fine-tune standard treatment by optimizing fluid therapy and use of vasopressor and inotropics. (3,4)
All data is saved for future reference as well as exportable to .cvs and Microsoft Excel for future reference and additional analysis.

Please visit MicroVision Medical at booth 79 at the 27th Annual Congress of the European Society of Intensive Care Medicine at the CCIM in Barcelona for a live demonstration of AVA 4.0 and automatically analyze your own sublingual microcirculation.

The AVA 4.0 version can be ordered now for existing MicroScan systems. Contact the MicroVision Medical Head Office at +31 20 566 5425 or mail to upgrade@microvisionmedical.com.
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www.microvisionmedical.com

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A GLANCE AT INTENSIVE CARE MEDICINE IN CHILE

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Chile is located in the south-western tip of South America, has 17.4 million inhabitants, and its population is growing at an annual rate of 0.9%. Chile has experienced significant economic development in recent decades, and it stands out amongst its South American neighbours for being a modern and democratic country with economic stability and active openness to globalisation, including free trade agreements with the largest economies. Per capita income has more than doubled over the past 20 years, becoming the highest in Latin America (OECD 2013).

Health in Chile has evolved in a manner roughly consistent with the gradual social and economic improvement that has occurred in recent decades (Pan American Health Organization 2010) (see Figure 1), including social policies focused on the most vulnerable population and the development achieved in the health system. The improved level of health is reflected in aspects such as life expectancy at birth greater than 78.5 years, a low maternal mortality rate (Ministry of Health, Chile 2008) (18.5 per 100,000 live births, see Figure 2) and a low infant mortality rate (9 per 1,000 live births), among the best in Latin America. Chile is also recognised for adequate control of infectious diseases, good sanitation and hygiene (OECD).

> *"The biggest challenge in Chile is to have the medical staff needed to run ICU units"*

This favourable outlook, however, faces the challenges posed by the particular geography of the country, with a long (4,329 km) but narrow (177 km average) surface that makes health coverage difficult in the more isolated areas. This is compounded by the striking income inequality: in Chile the top 20% of the population earn 13 times more than the bottom 20% (despite a relative poverty decline rate faster than any European country) (OECD 2013). Moreover, the progressive ageing of the population due to declining birth rates and an increasing life expectancy (OECD), together with the increasing complexity of medicine, have raised the demand for intensive care beds in the country.

This has led to a sustained growth in critical care beds, still insufficient for the increasing population and complexity. In the past 10 years critical care beds have increased from 773 to 1270, figures that include both ICU and intermediate care unit beds (Gálvez et al. 2013) (see Figure 3). Health investment in Chile has been constantly growing since the return to democracy, from 1.43% of GDP in 1980 to 6.7% in 2012; in that same period, critical care health investment has multiplied five times (Dirección de Presupuestos del Ministerio de Hacienda 2012). Chile seeks to further increase critical care bed availability in the next few years to reach 6 beds per 100,000 inhabitants, through both the building of new hospitals and the major equipment of existing hospitals. However, the biggest challenge in Chile is no longer the construction and equipping of new ICU units but to have the medical staff needed to run them (Gálvez et al. 2013).

Intensive Medicine in Chile

The first intensive care unit in Chile was established in 1968, within the Emergency Hospital, "Public Assistance", Dr.

Figure1. Gross Domestic Product and Life Expectancy (Chile 1995-2008)

Figure 2: Maternal Mortality Ratio in Chile (1960-2005)

Figure 3. National Availability of Physicians (Chile 1951-2012)

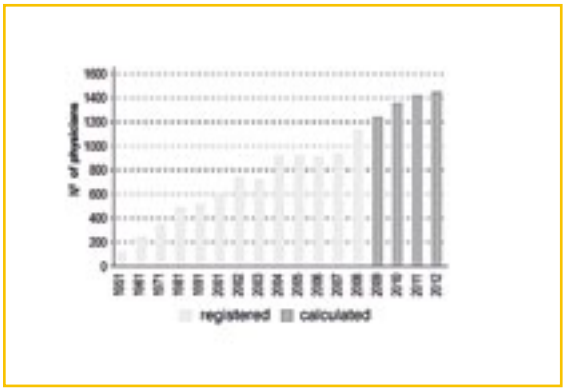

Figure 4. ICU and Intermediate Care Beds (Chile 2000-2012)

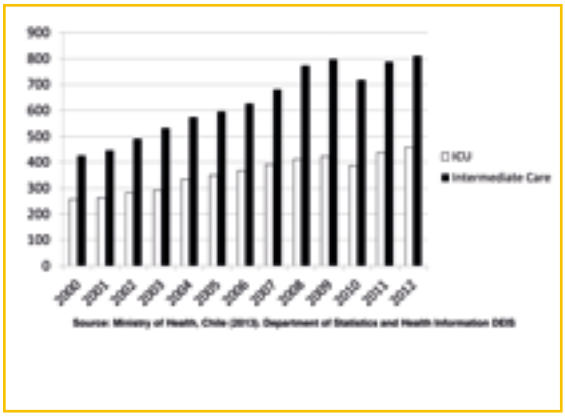

Figure 5: Physicians by Specialty in Chile, 2012

Statistics (2012)	
Total Population	17,465,000
Gross national income per capita (PPP International $)	21,310
Life expectancy at birth m/f (years)	77/83
Probability of dying aged under five (per 1,000 live births)	9
Total expenditure on health per capita (International $, 2010)	1,606
Total expenditure on health as a percentage of GDP	7.2

Source: World Health Organization Global Health Observatory http://www.who.int/countries/chl/en/

Alejandro del Río. This happened at the same time as the first coronary ICU was inaugurated in San Borja Hospital and fifteen years after Bjørn Aage Ibsen established the first ICU in Copenhagen in 1953.

Critical care medicine is a young specialty in Chile. The first Critical Care Scientific Society was founded in 1981, and critical care was formally recognised in 1987 as a specialty of medicine, yet it was not until 15 May 2001 that the Board of the National Autonomous Corporation of Medical Specialties Certification (CONACEM) completed the process of recognition of intensive care medicine and pediatric intensive care as specialties of their own (Medicina intensiva es reconocida por CONACEM como especialidad derivada 2001). The former is accessed in Chile as a derivative specialty of internal medicine, anaesthesiology or general surgery, whereas the latter is a derivative specialty of paediatrics. To access either of these two specialties, it is necessary to be certified by CONACEM in the corresponding basic specialty (Medicina intensiva es reconocida por CONACEM como especialidad derivada 2001).

Approximately 860 doctors currently work in intensive care units around the country with a shift system (Gálvez et al. 2013). Most are specialists in internal medicine, anaesthesiology or surgery, and a minority are intensive care medicine subspecialists. According to records from the Superintendent of Health, only 385 were certified specialists in 2012 (Ministry of Health, Chile 2008) (see Figure 4). The most conservative estimates by the Chilean Ministry of Health and the World Bank indicate that 736 certified specialists meet current demands (World Bank 2012). Until recently, only two Chilean universities offered intensive care as a specialty; this has recently increased to five universities, but even so, only 10 specialists currently graduate every two years. Given the speed of training of specialists, this means that several decades would be required to meet the demands of all ICU units in the country. And so: what we can do?

Chilean scientific societies, universities and health authorities have been discussing various models of university education based on competencies, including the possibility that other specialties, including emergency medicine, neurology, obstetrics and neurosurgery, can access intensive medicine training programmes as a subspecialty. The possibility of providing intensive care medicine as a primary specialty, as in Spain or Argentina, is also being discussed. Simultaneously, scientific societies are making a huge effort to continue to provide medical education for physicians already working in ICUs, who are not certified in intensive care, as a way to standardise care around the country. Both strategies appear to be necessary and complementary to meet the country's needs. ■

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

Scientific Societies are making a huge effort to continue to provide medical education for physicians and professionals working in ICUs.

EXTRACORPOREAL CARDIOPULMONARY LIFE SUPPORT: THE EXPERIENCE WITH ECMO IN CHILE

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ECMO (extracorporeal membrane oxygenation) is an increasingly common system of extracorporeal life support in catastrophic pulmonary failure, acute heart failure and resuscitation. ECMO allows the heart and/or lungs time to rest and heal, providing opportunity for recovery. Technological advances have made ECMO devices smaller, less invasive, and easier to use. Chile has implemented this technology in different hospitals, with results comparable to international registries.

Although ECMO therapy in adult patients was incorporated several decades ago in Chile, this practice was scarce and limited to a few centres with a small number of annual cases. Therefore during the 2009 H1N1 pandemic the results of its use were disappointing. In a study we found that overall survival was 75% of those treated with High-Frequency Oscillatory Ventilation (HFOV) and only 40% of those treated by ECMO (Ugarte et al. 2010). At that time we believed that implementation of this complex technique should be reserved for well-trained and experienced centres, and we showed that transport of patients needing ECMO used to be technically impossible, even after hours working at the bedside with the ventilator, sedation, and relaxation parameters (Ugarte et al. 2010).

> *"Chile has implemented this technology in different hospitals, with results comparable to international registries"*

Now, a few years afterwards, ECMO centres have increased fourfold. Units with well-established ECMO programmes have a lower threshold for ECMO. Extracorporeal membrane oxygenation also necessitates high-risk transports to specialised centres, when retrieval on ECMO is not possible. Now when the candidate to be submitted is too unstable to be transported to a hospital with ECMO, cannulation in site allows the stabilisation and transfer to a facility with well-established ECMO programmes for extracorporeal oxygenation. In a recent study in 2013, performed in three ICUs in the same centre, we showed that, during the study period, of the 351 patients admitted to the three ICUs, 150 of them required mechanical ventilation, 26 HFOV, and 5 patients received ECMO. We documented an overall survival of 80%, with 5.5 days in ECMO (Ceballos et al. 2013). A study of an ECMO transport programme now reported an overall survival in the ECMO group of 64%, with 7.7 (+ 5.9) days on ECMO, and 29.7 (+ 26.2) days of ICU length of stay (Díaz 2011). These results are both comparable to the Extracorporeal Life Support Organization (ELSO) registry reports [http://www.elsonet.org].

On the other hand the first Chilean neonatal / paediatric ECMO programme was started 11 years ago. When comparing the period before and after the establishment of this programme of ECMO in Chile, it was found that the survival of the total group of infants with severe respiratory failure (Oxygenation Index > 25) increased significantly from 75% (75/100) in the pre-ECMO period to 91% (67/74) in the ECMO period (Kattan et al. 2013). During the ECMO period, 70% of these patients with severe

respiratory failure were rescued with nitric oxide and / or high frequency oscillatory ventilation (HFOV), while 30% did not improve, and 76% of these received ECMO (Kattan et al. 2013).

A recent study of 51 paediatric patients connected to ECMO between May 2003 and August 2013 (39 respiratory, 12 cardiac) showed positive overall outcomes: 74% of respiratory ECMO and 83% of Cardiac ECMO survived ECLS (Castillo et al. 2014), similar to the international literature.

Currently Chile has eight centres with ECMO programmes for both adults and paediatric patients. Two centres are in the public health sector and six in private hospitals, and all are geographically located at the centre of the country. According to the records of the ELSO, throughout the rest of Latin America there are nine centres with ECMO programmes: four centres in Argentina, three in Brazil, one in Colombia, and one centre in Mexico (Extracorporeal Life Support Organization). In recent years Chile has increased transport of patients to receive this therapy. Controversy still persists over the use of ECMO in countries with limited resources, and now health authorities, together with scientific societies, are looking to establish a network of management of these patients with well-defined indications, and protocols of referral and management. Veno-venous ECMO represents a significant escalation of support rather than a mere substitution for lung protective ventilation, and careful patient selection is key to its success.

Despite some evidence of it being cost-effective, authorities and experts are concerned that running the service in several nearby centres outside a pandemic context may lead to inadequate exposure, infrequent training opportunities, and questionable cost-effectiveness. Centralising ECMO services to ICUs with well-established ECMO programmes may improve results and cost-effectiveness, especially when the actual requirement for ECMO outside the influenza pandemics itself is expected to be low (1-2 cases per million population annually) (ECMO Expert Group 2010). Pending further evidence, ECMO may have to be considered, and early referrals may be made to an ECMO-equipped centre for patients with severe acute respiratory failure, where no contra-indications exist. This, by itself, may improve outcomes, as demonstrated in the CESAR study (Peek et al. 2009).

We hope that these new ECMO referral centres, associated with better network management, will impact positively on the survival of patients with respiratory or cardiac failure, and increase the availability of this expensive therapy in the future to a greater number of patients in our country. The ECMO therapy, now more broadly called "extracorporeal life support" (ECLS) therapy is currently available in Chile, with proven benefits in the short and long term. The Chilean experience shows that it is possible to progressively incorporate it with success in the practice of critical care in developing countries, but it needs to be implemented in high-complexity centres, with well trained personnel and with a high level of commitment. ■

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AGENDA

OCTOBER

1 - 3	The 28th Paediatric Intensive Care Society Conference (PICS 2014) Newcastle, UK www.picsmeeting.com
9 - 10	Biomarker Europe Summit Dublin, Ireland www.gtcbio.com/conferences/biomarker-europe-summit-2014-overview
9 - 11	ANZICS/ACCCN Intensive Care ASM Melbourne, Australia www.intensivecareasm.com.au/2014/
17 - 21	5th Congress of the European Academy of Paediatric Societies - EAPS Barcelona, Spain www2.kenes.com/eaps
22 – 25	WSC (World Stroke Congress) Istanbul, Turkey www.worldstrokecongress.com
29 Oct. – 1 Nov.	Critical Care Canada Forum Toronto, Canada www.criticalcarecanada.com

NOVEMBER

13 - 16	4th Eurasian Congress on Emergency Medicine Antalya, Turkey www.eacem2014.org
14 - 15	ESA Focus Meeting on Perioperative Medicine: The Paediatric Patient Athens, Greece www.esahq.org/congresses/focus-meeting-2014
18 - 20	Echocardiography for Hemodynamic Monitoring 2014 Brussels, Belgium www.intensive.org
24 - 26	Cardiorespiratory Physiology Postgraduate Refresher Course Brussels, Belgium www.intensive.org
24 – 28	4th World Congress of Regional Anaesthesia & Pain Therapy (WCRAPT 2014) Cape Town, South Africa www.wcrapt2014.com
27 - 29	4th International Fluid Academy Days Antwerp, Belgium http://imerit.org/ifad/
26 - 30	Critical Care Congress 2014 - Inspiring ICU Cape Town, South Africa www.criticalcare.org.za/CritCare14_FirstAnnounce.asp

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ESICM Appointed Chair: Antonio Torres (Barcelona, Spain)

Program

12:30–12:40 **Introduction – Why Rapid and Accurate Diagnosis Matters**
Mervyn Singer (UK)

12:40–13:00 **Diagnostic Challenges of Critically Ill Patients**
Mark Wilcox (UK)

13:00–13:20 **The Impact of Diagnostics on Patient Care**
Tobias Welte (Germany)

13:20–13:50 **RADICAL – A Multicenter Study Demonstrating Benefits of Rapid Diagnostics Using PCR/ESI-MS**
Jean-Louis Vincent (Belgium)

13:50–14:00 **Conclusions and Q&A**
Mervyn Singer (UK)

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