ICU MANAGEMENT

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Organ Donation

PLUS:

- Respiratory Monitoring in the Perioperative Period
- Intelligent Ventilation in the ICU: Technology Improving Patient Outcomes
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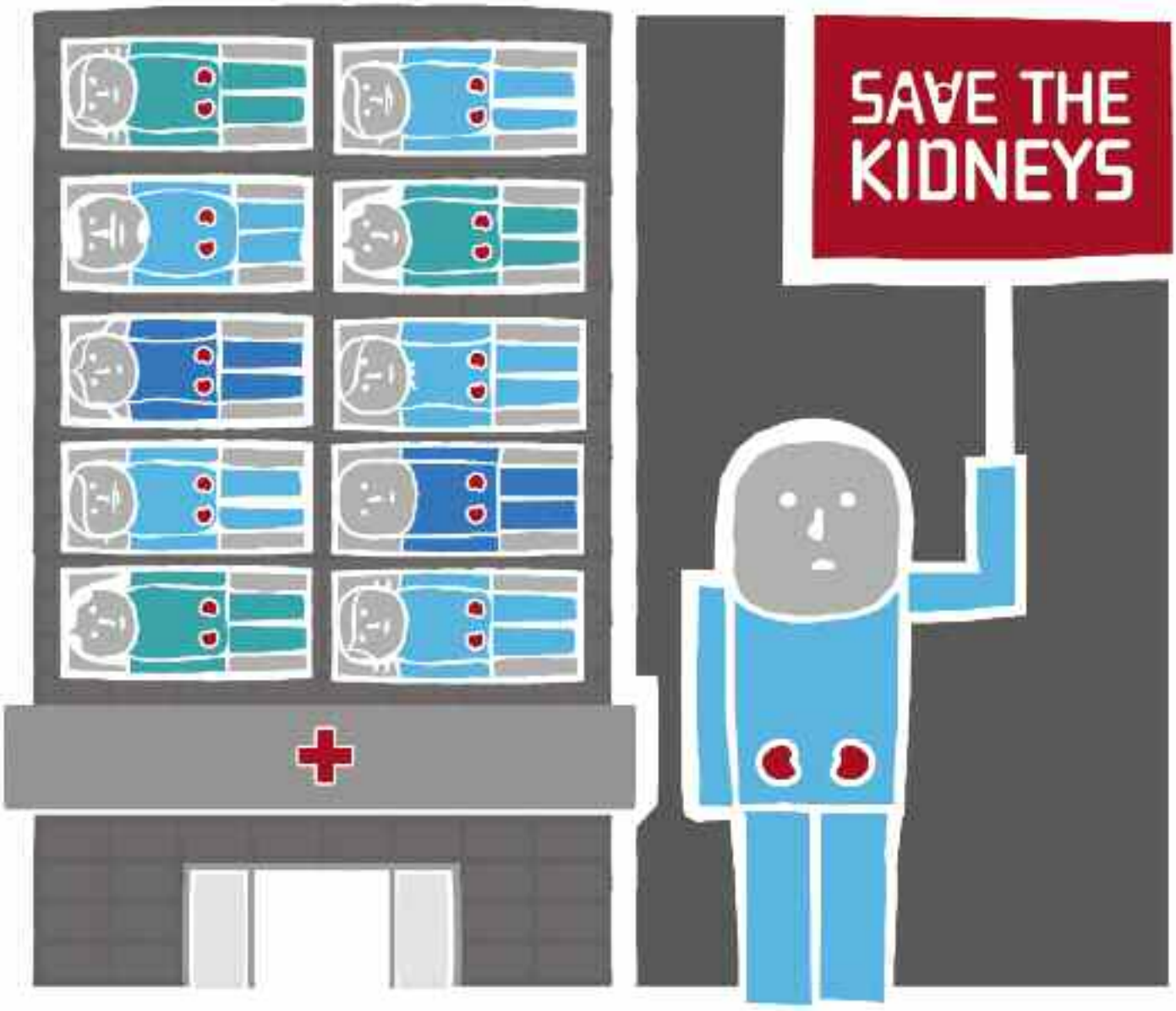

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ORGAN DONATION

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With thousands of patients dying from lack of donor organs every day, the topic of organ donation is a timely one. With ICUs often the location for the beginning of this process, our cover story focuses on this topic. Even without considering the loaded subject of the politics of 'opt-in' or 'opt out' systems of organ donation, there is much that can be done to improve the rate of organ donation.

Dr. Teresa Pont writes about implementing the concept of self-sufficiency, the critical pathway for organ donation after death, and including the option to donate as part of end-of-life care. She argues that the option of donation is an ethical commitment in end-of-life care.

Dr. Jonathan Ball writes about the optimal management of the potential donor patient following catastrophic brain injury, suggesting that more can be done to optimise organ function before assessment and retrieval, and he outlines best practice for this.

Prof. David Crippen and Prof. Leslie Whetstine argue the pros and cons of uncontrolled organ donation following cardiac arrest outside the hospital setting. Prof. Crippen proposes that preserving organs for organ donation early on while awaiting consent is ethically neutral and reasonable. Prof. Leslie Whetstine argures that uncontrolled donation after circulatory determination of death is ethically and medically specious.

Next, in our Matrix section, Dr. Yuda Sutherasan and colleagues look at the important topic of respiratory monitoring in the perioperative period, considering the tools available as well as monitoring in specific conditions. This is followed by Prof. David Linton and colleagues' clinical experiences over the past decade of intelligent ventilation.

The European Society of Anaesthesia's patient safety starter kit is the subject of Prof. Sven Staenders piece. The kit was launched at ESA in June, and the societies have a comprehensive plan to disseminate it with the goal of implementing the Helsinki Declaration on Patient Safety in Anaesthesiology.

Prof. Preiser and colleagues write about indirect calorimetry. Their article explores the different uses and clinical relevance of using indirect calorimetry to manage caloric prescription in critically ill patients. They consider the evidence and ask: is it an essential tool to optimise nutrition or more suited as a research tool?

In our Management section, Dr. Lascarrou and colleagues look at the topic of delayed admission to the ICU, and consider the causes. Given that most countries do not have enough ICU beds, it is important to look at reasons for delays.

Prof. Djillali Annane kindly found time to speak to us for our interview section. Prof. Annane's research interests focus on sepsis, and he talks about the preliminary findings of the CRYSTAL study as well as his thoughts on fluid resuscitation, the role of clinical trials in the future, current hot topics and important breakthroughs.

Our country profile this issue is South Africa, and we are delighted to have talked to Dr. Dean Gopalan and Prof. Satish Bhagwanjee, co-chairs of the organising committee of the 11th Congress of the World Federation of Societies of Intensive and Critical Care Medicine, which will take place in Durban, South Africa, August 28th - September 1st 2013.

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

Jean-Louis Vincent

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INDUSTRY AND RESEARCH NEWS

Supension of Hydroxyethyl-Starch Solutions to be Re-Examined

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has concluded that the benefits of infusion solutions containing hydroxyethyl-starch (HES) no longer outweigh their risks, and recommends that the marketing authorisations for these medicines be suspended.

The review was triggered following three recent studies that compared HES with crystalloids in critically ill patients, which showed that patients with severe sepsis treated with HES were at a greater risk of kidney injury requiring dialysis. Two of the studies also showed that in patients treated with HES there was a greater risk of mortality. The PRAC was requested by the German medicines agency, the Federal Institute for Drugs and Medical Devices (BfArM), to assess the evidence and how it impacts on the risk-benefit balance of HES infusion solutions in the management of hypovolaemia and hypovolaemic shock.

The PRAC assessed data from the scientific literature and data submitted by the companies, and took advice from a group of external experts. The PRAC considered that, when compared with crystalloids, patients treated with HES were at a greater risk of kidney injury requiring dialysis, and had a greater risk of mortality. The PRAC also considered that the available data only showed a limited benefit of HES in hypovolaemia, which did not justify its use considering the known risks. The PRAC therefore concluded that the marketing authorisations for these medicines be suspended.

As these medicines are all authorised nationally, the PRAC recommendation will be forwarded to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a final position. The CMDh is a medicines regulatory body representing the EU Member States. If the CMDh position is agreed by consensus, the agreement will be directly implemented by the Member States where the medicines are authorised. Should the CMDh position be adopted by majority vote, the CMDh position will be sent to the European Commission, for the adoption of an EU-wide legally binding decision.

Following the recommendation, some of the marketing authorisation holders have requested a re-examination. On receipt and validation of the grounds, the PRAC will re-examine its recommendation and issue a final recommendation. The recommendation will remain in place unless the marketing authorisation holder can provide convincing data to identify a group of patients in whom the benefits of the medicines outweigh their risks. The outcome is expected in the autumn, and will be made public on the EMA website (www.ema.europa.eu).

In the UK the Faculty of Intensive Care Medicine, the Royal College of Anaesthetists, the Intensive Care Society and the College of Emergency Medicine have issued a position statement outlining approaches to fluid therapy pending a definitive decision by the regulatory authorities (www.collemergencymed.ac.uk)

Prone Positioning in Severe ARDS: PROSEVA Results

The Proning Severe ARDS Patients (PROSEVA) Study Group recently published impressive results in the New England Journal of Medicine. This multi-centre, prospective randomised controlled trial looked at the role of prone positioning in patients with early, severe ARDS during mechanical ventilatory support.

Patients were recruited from 26 ICUs in France and one in Spain, all of which have used prone positioning for more than five years. 466 patients were randomly assigned to the supine position or to undergo prone positioning sessions of at least 16 hours. 229 patients were assigned to the prone group, and 237 patients to the prone positioning group. All were treated in standard ICU beds.

At 28 days mortality was 16% in the prone group and 32.8% in the supine group. Secondary end points were mortality at day 90, the rate of successful extubation, time to successful extubation, length of stay in the ICU, complications, use of noninvasive ventilation, tracheotomy rate, number of days free from organ dysfunction, and ventilator settings, measurements of arterial blood gases, and respiratory-system mechanics during the first week after randomisation. The rate of successful extubation was significantly higher in the prone group. The significant difference in mortality persisted at day 90, while the duration of invasive mechanical ventilation, length of stay in the ICU, incidence of pneumothorax, rate of use of noninvasive ventilation after extubation, and tracheotomy rate did not differ significantly between the two groups.

The authors suggest that several factors may explain their results. Patients with severe ARDS were selected on the basis of oxygenation together with PEEP and Fio2 levels. Secondly, patients were included after a 12-to-24-hour period during which the ARDS criteria were confirmed. This period may have contributed to the selection of patients with more severe ARDS who could benefit from the advantages of prone positioning, such as relief of severe hypoxemia and prevention of ventilator induced lung injury. In addition the trial used long prone positioning sessions, the prone position was in place for 73% of the time ascribed for the intervention, and was concentrated over a period of a few days. The tidal volume was lower than in previous trials, and the PplatRS was kept below 30 cm of water. The authors acknowledge that because all patients were returned to the supine position at least once a day, the effect of the prone position itself cannot be distinguished from the effects of being moved from the supine to the prone position over the course of a day.

The technical aspects of prone positioning are covered by two videos provided by the authors on the NEJM website (www.nejm.org).

In an accompanying editorial, Guy W. Soo Hoo comments, "There can no longer be any doubt. Prone ventilation in selected patients with severe ARDS has arrived and is ready for its turn in the management of the disease."

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CRITICAL CARE FOR ALL

PROVIDING MORE FOR LESS

DONATION AS AN ETHICAL COMMITMENT IN END-OF-LIFE CARE

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Thousands of patients are waiting for the phone call announcing that they may have a chance to live longer, better, or just to live. Organ donation has changed the lives of millions by pushing the limits of medical treatment; limits that transcend the death of one person and extend the life of another. Not surprisingly, several ethical considerations arise in this complex scenario, which represent the substance of the recently developed international standards that this paper comments on.

Donation and Transplantation in the Global Landscape

Organ transplantation depends on the availability of human organs. Their scarcity means there is a waiting list of almost 60,000 in the European Union (EU) (Council of Europe 2012) and over 118,000 in the USA (Organ Procurement and Transplantation Network 2013). It has been estimated that 12 patients die on the waiting list each day in the EU. Recent statistics show that deceased donation rates vary dramatically, from 35.2 per million population (pmp) in Spain to 0.6 pmp in Japan, with many countries not registering any deceased donation activity at all (DOPKI 2009). Comparisons are also difficult when organisations only provide minimal figures about transplantation results.

> *"Giving and receiving are inherent to human life, and organ donation and transplantation are based on these cornerstones of survival"*

Diversity in organ donation and transplantation rates activities in the EU is highlighted by data collected within several EU-funded projects (DOPKI 2009). Variability in rates of donation after death between EU Member States is not seemingly due to differences in mortality rates or in public support for organ donation. On the contrary, differences in the organisational approach might be the underlying reasons for these variations (DOPKI 2009).

The disparity between supply of, and demand for, transplantable organs has triggered a wide variety of initiatives, as discussed at The Third World Health Organization (WHO) Global Consultation on Organ Donation and Transplantation, held in Madrid on March 23 to 25 of 2010, where there was a call for a comprehensive national strategy based on self-sufficiency in transplantation (WHO 2011).

Implementing the Concept of Self-Sufficiency

As specified in the Madrid Resolution, self-sufficiency means the capacity to meet patients' transplantation needs founded on each country's own resources, aiming to foster the adequate provision of organ and transplantation services to a given population, including international cooperation when appropriate. Self-sufficiency implies the maximisation of donation, making donation possible in all circumstances of death, a principle already stressed in the WHO Guiding Principles for the transplantation of human organs, tissues and cells (WHO 2010).

The Madrid resolutions develop many recommendations and requirements regarding emergency and intensive care departments, by increasing skills, awareness, collaboration, and support for donation from the deceased. Equally important is the defini-

tion of their critical role in better identifying possible and potential donors and the elaboration of standards, unambiguous guidance and protocols on how to manage the dying process. Hence, donation must be included as part of end-of-life care and is regarded as the responsibility of all healthcare professionals involved.

The Critical Pathway for Organ Donation After Death

Donor detection is the key factor preceding the step of organ referral. Up to 60 percent of patients with a devastating brain injury derived from stroke, trauma, or cardiac arrest die after family members and clinicians, given the poor prognosis, decide that further treatment is futile, without considering donation (Sprung et al. 2003). Outcomes after these decisions are very difficult to predict with certainty, and in the face of value-laden decisions and prognosis, treatment-withdrawal practices vary widely (Decato et al. 2013). However, it is surprising that there are practically no published studies regarding the number of brain deaths in these pathologies.

A systematic approach to the process of donation from deceased persons will help populations to define actions, roles and responsibilities in both donations after brain death (DBD) and donations after circulatory death (DCD). The critical pathway delivered in the Madrid Conference of 2011 (Transplantation 2011) is:

a) To provide a common systematic approach to deceased donation;
b) To create a common trigger to facilitate the prospective identification and referral of potential deceased donors and precipitate the deceased donation process, and
c) To provide common procedures to estimate potential organ donation from deceased persons and to evaluate performance in the process of donation after death (Domínguez-Gil et al. 2011).

The pathway stipulates that any patient with a devastating brain injury, i.e. Glasgow Coma Scale below 5 (Council of Europe 2010) or with circulatory failure, who is apparently suitable for organ donation, must be considered for organ donation as part of end-of-life care. Above all, the dead donor rules must be respected (Transplantation 2011), that is, patients may only become donors after death, and the recovery of organs must never cause a donor's death (De Vita et al. 2007).

It is strongly recommended to refer every case to transplant coordinators for further evaluation, in order to inform families about donation when futility of treatment is independently decided by the team in charge (De Vita et al. 2007); Daly et al. 2006).

Option to Donate as Part of End-of life Care

Giving and receiving are inherent to human life, and organ donation and transplantation are based on these cornerstones of survival. These basic survival mechanisms are developed within a relational context and specific cultural conditions. Based on these principles, organ and tissue donation means gifting one's heritage

to whoever needs it.

The option of organ donation must be considered as an integral part of end-of-life care and occurs as the culmination of two processes: the ending of a patient's life and the gaining of permission for donation from the patient or the patient's family (Daly et al. 2006). Donation cannot occur outside this context, and thus understanding end-of-life issues and committing to a caring request process are essential. However, this is a complex and extremely stressful situation for all those involved, which demands total honesty and respect. Easier said than done! (Masnou and Pont 2012; Truog et al. 2008; Shafer et al. 2008).

> **"It is, indeed, most difficult to do things that are beneficial and good"**
> *Dhammapada, XII, 163. Buddha*

Hence, the ability to provide sensitive and technically competent care to dying patients and their families is a prerequisite to the success of all donation programs (Truog et al. 2008; Jacoby et al. 2006).

Professional education in precisely how to manage these difficult situations with empathy and tact is full of gaps (Pont et al. 2008), making ethical discussion even more complex and necessary. Lack of adequate training to raise awareness in medical staff has been shown to be the cause of lower donor detection and referral rates (Hart et al. 2012). The literature reviewed consistently shows that where the process was coordinated and managed the consent rates were improved (Shafer et al. 2009; Shafer et al. 2008).

Summary

- Quality end-of life care is "best provided through the collaborative practice of an interdisciplinary team to meet the physical, emotional, social and spiritual needs of the person and their family" (Canadian Hospice Palliative Care Association 2002);
- Improving end-of-life care and increased organ donation are essential goals formally recognised by healthcare professionals and by society at large;
- The option of donation is an ethical commitment in end-of-life care. ■

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OPTIMAL MANAGEMENT OF THE POTENTIAL ORGAN DONOR FOLLOWING CATASTROPHIC BRAIN INJURY

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This article presents best practice in organ donation, aimed at maximising organs that can be retrieved and optimising graft function and survival. Failure to optimise organ function prior to assessment and retrieval should and can be avoided.

Introduction

Except in exceptional circumstances, cadaveric solid organ donation occurs following catastrophic brain injury (CBI). Cadaveric solid organ donation is highly successful and enjoys broad public and professional support. However, there is a significant, and worsening, supply-demand imbalance. In this context, it is appropriate, morally, ethically and economically, to ensure that no opportunities are missed. Common avoidable causes of missed opportunities include failures to:

- Consider organ donation, once the clinical decision has been made that continuing supportive care has no realistic prospect of achieving a meaningful functional recovery for the patient;
- Continue organ support until the patient's wishes with regard to organ donation can be established;
- Establish a diagnosis of brainstem death (BSD);
- Discuss with, and gain consent for, organ donation, with the patient's next of kin; and
- Optimise organ function prior to assessment and retrieval, especially of thoracic organs (Statistics and Clinical Audit).

The first four issues remain both challenging and controversial (Randall and Downie 2012; Neuberger 2012). However, there is emerging, and I believe, compelling evidence that should remove the fifth item from this list. In this article, I will attempt to present both the specific elements that constitute current best practice and the evidence that this package of care is effective in increasing the chances of successful donation, maximising the number of organs that can be retrieved and optimising both graft function and survival (Minambres et al. 2013; Hagan et al. 2009; Franklin et al. 2010; Malinoski et al. 2013; Malinoski et al. 2012).

This article is based upon practices and legislation in the United Kingdom. There are significant differences between these and those of other countries, a topic recently reviewed by Bilgel (Bilgel 2013).

A Clinical Scenario

A 45-year-old man suffers an isolated, severe traumatic brain injury. He has been intubated and ventilated, computed tomography scanning has been completed from vertex to mid thigh, immediate resuscitation has been completed together with a full secondary survey, following which he is transferred to ICU. Despite optimal care and minimisation of secondary brain injury, the intracranial pressure remains persistently elevated. The clinicians reach a consensus that there is no realistic prospect of achieving a meaningful functional recovery for the patient.

Three processes should now be simultaneously instituted:

1. Confirmation or refutation of the diagnosis of BSD. BSD should be suspected if there are fixed and dilated pupils, a Glasgow coma score of 3/15, an absence of triggering / patient interaction with the mechanical ventilator, and the absence of any potentially reversible cause for these clinical findings. In the UK, the reversible causes are detailed in *A code of practice for the diagnosis and confirmation of death* (Academy of Medical Royal Colleges, 2008) and listed in Table 1. Thus, the first steps may be cessation of all depressant and neuromuscular blocking drugs, and rewarming to ~35°C, if therapeutic hypothermia has been instituted. Of note, there is a small but significant incidence of complex-spontaneous motor movements and false-positive triggering / interaction with the ventilator in patients who are brain dead (Wijdicks et al. 2010). Examples of the latter usually occur due to the high sensitivity of modern ventilators and represent cardiovascular triggering (Arbour 2012; McGee and Mailloux 2011). Failure to be aware of these phenomena can result in significant delays in confirming brain death.
2. Physiological optimisation should be initiated / continued, both to enable BSD testing and maximise the potential for heart, lung, kidney, liver and other organ

transplantation (for the suggested timeline see Figure 1, p.13). This is considered controversial by some, who argue that it is not in the patient's best interests. However, failing to do this may delay or prevent BSD testing and will result in worse outcomes, if organ donation proceeds, which can only occur if it is in accordance with the patient's wishes. If consent or other issues subsequently preclude organ donation then withdrawal of organ support should be undertaken at a time, and in a manner, that is consistent with best practice in end-of-life care. In addition, from a societal perspective, it can reasonably be argued that following the confirmation of BSD, you are no longer treating the donor but instead are treating multiple recipients.

3. Establish whether there are any absolute contra-indications to organ donation (medical and/or legal), and whether the wishes of the patient have been registered and/or are known to the next of kin.

Physiological Optimisation Following CBI

Severe brain injury is commonly associated with a multiple organ dysfunction syndrome, characterised by a systemic pro-inflammatory state and endogenous catecholamine excess. Neuro-critical care practices may have added to this physiological derangement by inducing a state of relative hyperosmolar, hypovolaemia, with high systemic arterial pressures, hyperoxia, hyperventilation / hypocarbia and suboptimal positive end expiratory pressure (PEEP). If this progresses to BSD, a highly variable, autonomic and endocrine, failure syndrome occurs, which in the majority of cases, results in cardiovascular instability and a further deterioration in the function of all other organs (Bugge 2009). This multiple organ dysfunction syndrome often abates within a 6-24 hour period if actively managed. In this setting, physiological optimisation merely represents routine (best practice) critical care. A summary of targets, tests, drugs and procedures is shown in Table 2. Notes regarding specific elements of this care package are outlined below.

Table 1. Potentially Reversible Causes of Unresponsive Coma and Apnoea (Academy of Medical Royal Colleges 2008)

- Depressant drugs
- Core temperature ≤34°C
- Obvious reversible circulatory, metabolic or endocrine cause
- Neuromuscular blocking agents or other reversible causes of apnoea
- Blood levels
  - Sodium <115 or >160mmol/L
  - Potassium <2mmol/L
  - Phosphate <0.5 or >3.0mmol/L
  - Magnesium <0.5 or >3.0mmol/L
  - Glucose <3.0 or >20.0mmol/L

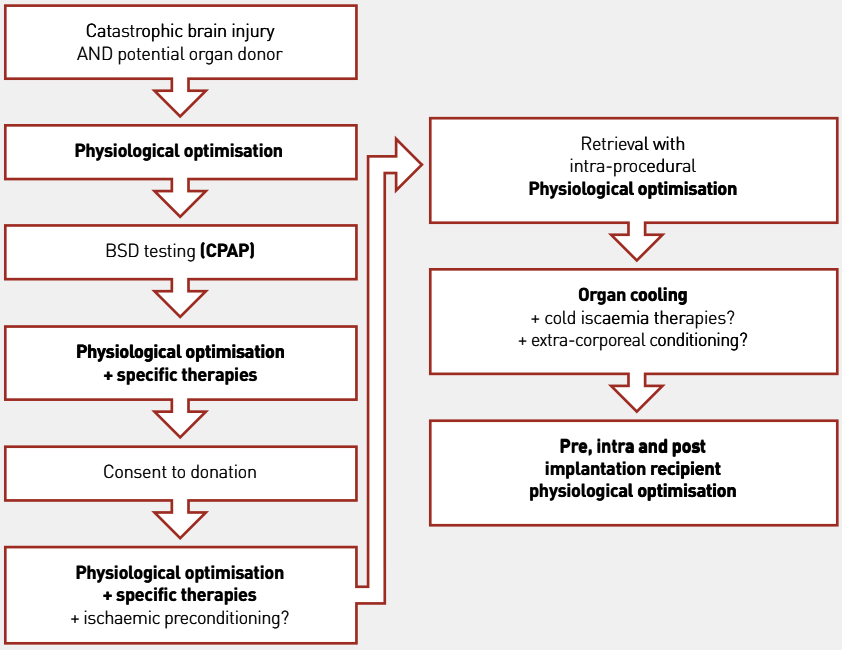
Respiratory system

- Standard lung protective ventilation (Kilickaya and Gajic 2013) should be

Table 2. A Summary of Targets, Tests, Drugs and Procedures

Airway - endotracheal / tracheostomy tube
Distal tip of the tube is located in the mid / lower trachea • Recent chest x-ray • Reported by senior clinician • No cuff leak and cuff pressure is ~32cmH_2O • Urgent sputum Gram stain & microscopy • Continue 6hrly oral chlorhexadine
Breathing & Blood tests
Set (and measured) positive end expiratory pressure (PEEP) 8-10cmH_2O • Perform recruitment manoeuvre (repeat as indicated) • Arterial oxygen tension (PaO_2) 8-14kPa • and / or • SpO_2 92-95% • on minimum FiO_2 • Tidal volumes (Vt) 6-8ml/kg (ideal body weight) • Peak (plateau / end inspiratory) pressure ≤30cmH_2O • Arterial carbon dioxide tension ($PaCO_2$) 5.0-6.5kPa • Respiratory rate and I:E ratio set to achieve target $PaCO_2$ and prevent dynamic hyperinflation • Send blood for: full blood count • clotting screen • group and save for transfusion • renal / liver / bone / cardiac biochemistry • virology • tissue typing
Circulation and blood Composition
Rate & rhythm: Sinus rhythm 60-100 bpm • 12 lead ECG • Reviewed & reported by senior clinician • ***Preload:*** stroke volume index (SVI) 33-47 ml/m^2/beat • and / or • stroke volume variation (SVV) <15% • and / or • CVP 8-12mmHg • ***Contractility:*** Cardiac index (CI) ≥2.4 l/min/m^2 • Echocardiogram (if possible) • ***Afterload:*** Mean arterial pressure (MAP) 60-80mmHg • and / or • systemic vascular resistance index (SVRI) 1800-2400dynes • sec/cm^5/m^2 • ***Global oxygen supply demand balance:*** Central venous oxygen saturation (ScvO2) ≥60% • and / or • mixed venous oxygen saturation (SvO_2) ≥70% • and / or • Central venous-to-arterial carbon dioxide difference (Pcv-aCO_2) ≤0.8kPa • ***Blood composition:*** [Hb] ≥80g/l • Platelets >50x10^9/l • INR <2.0 • APTT ratio <1.5 • fibrinogen >2.0g/l • ***Vascular access:*** reliable large bore intravenous access • arterial line • central venous line
Dextrose & drugs
Blood glucose 4.0-10.0mmol/l • Insulin infusion ≥1iu/hr • 20% dextrose infusion at 25ml/hr (or alternative) • Give 15mg/kg methylprednisolone IV • repeat every 24 hours
Electrolytes & environment
Na^+ 135-150mmol/l • K^+ 4.0-5.5mmol/l • Mg^{2+} >0.8mmol/l • Ca^{2+} 1.0-1.3mmol/l (ionised) • or 2.0-2.6mmol/l (total) corrected for albumin • PO_4^{3-} >0.8mmol/l • Core temperature 35.5-37.5°C • Maintain 30-45° head of bed elevation • VTE prophylaxis: LMWH • TED stockings • +/- calf compressors
Fluid balance (renal)
No maintenance fluids • urine output 0.5-2.5ml/kg/hr • (***if less*** → ensure circulation optimised and catheter patent; ***if more*** → ensure adequate replacement / euvolaemia / normonatraemia AND test for +/- treat diabetes insipidus (DI)

Figure 1. A Suggested Timeline for Physiological Optimisation Following Catastrophic Brain Injury and Suspected BSD.



employed and is of proven benefit in this patient population (Van Raemdonck et al. 2009, Minambres et al. 2013, Mascia et al. 2010). This should include regular assessment of lung recruitability and PEEP optimisation (Minambres et al. 2013, Jauncey-Cooke et al. 2009).

- Airway pressure release ventilation may be beneficial, (Hanna et al. 2011) but only if the clinicians caring for the patient are familiar with its use.
- Apnoea testing should be conducted using continuous positive airway pressure (CPAP) (Mascia et al. 2010). This can easily be achieved without disconnection from the ventilator, either by disabling apnoea backup and/or switching to a non-invasive setting.
- Exposure to hyperoxic gas mixtures should be minimised (Kallet and Matthay, 2013).

Cardiovascular system

- Cardiovascular instability may develop rapidly due to:
  - hypovolaemia secondary to diabetes insipidus;
  - myocardial depression due to catecholamine and cytokine toxicity;
  - the transition from hypertensive catecholamine excess into vasoplegic hypotension.

> *"It is appropriate, morally, ethically and economically, to ensure that no opportunities are missed"*

Hence, invasive blood pressure and cardiac output monitoring is essential. Management should employ standard methods for optimisation of the circulation. Recommended physiological targets are shown in Table 2. There are however, a few points worth emphasising.

- Fluid (and electrolyte) management can be especially challenging and benefits from senior review. The trade-off between euvolaemia with adequate organ perfusion and organ oedema (especially lung) must be actively managed. Central venous pressure cannot be relied upon as a marker of preload (Durairaj and Schmidt 2008).
- Myocardial stunning is a common observation following BSD but may reverse with optimal supportive therapy, albeit over a 24-48 hour period (Casartelli et al. 2012, Christmas et al. 2012).
  - Low dose dobutamine (2.5μg//kg/min) may be beneficial in ameliorating ex-vivo, cold ischaemic injury (Benito et al. 2004) but high doses may deplete high energy phosphates.
  - Some cardiothoracic transplant units encourage the use of thyroid replacement therapy for all donors. Trial evidence (Macdonald et al. 2012) suggests it may add little to active donor management and is not necessary routinely. There is also anecdotal evidence of a small but significant incidence of cardiac toxicity if routinely used. Thus, thyroid replacement therapy should be considered as a second line positive inotrope in patients with myocardial depression (Ranasinghe and Bonser, 2010).
- Vasopressin (or terlipressin) should be used as the first line vasopressor. The addition of norepinephrine may be required. Vasopressor resistance may be encountered and may respond to hydrocortisone, which should be given regardless of whether or not methyprednisolone has been given (see below). The rationale for this approach is based on the mineralocorticoid effects of hydrocortisone (Druce et al. 2008) (methylpredisolone has no mineralocorticoid action).
- Markers of global oxygen supply demand balance are valuable physiological targets, however the following should be noted.
  - Arterial / central venous lactate measurements may be elevated despite optimal oxygen delivery as high levels of catacholamines, endogenous or exoge-

nous (especially ß2 agonists) increase production beyond the elimination threshold. In addition, the injured brain may produce significant amounts of lactate.

- ScvO2 has a number of important pitfalls (Barbee et al. 2010). A low (<70%) central venous oxygen saturation (ScvO2) may be improved by packed red blood cell transfusion, but this has potentially negative consequences, in particular related to transfusion related immunomodulation. Hence it is best to discuss the pros and cons with the organ donation co-ordinator.
- Central venous-to-arterial carbon dioxide difference (Pcv-aCO2) may be a useful additional target (Vallee et al. 2008).

Endocrine therapies and donor immunosuppression

- The incidence and clinical impact of functional hypothyroidism and hypoadrenalism remain controversial. Universal use of blind therapy is at best of no benefit and may be harmful. However the use of tri-iodothyronine and / or hydrocortisone may be beneficial in some individuals (see above).
- Acute posterior pituitary failure is very common, results in diabetes insipidus (DI) and is a major contributor to vasoplegic shock. Hence, vasopressin (or terlipressin) are recommended as first line vasopressors whilst simultaneously treating DI.
- Insulin is recommended for all potential organ donors and has myriad potential beneficial effects, though evidence of these from well designed and conducted randomised control trials is lacking.
- Methylprednisolone at a dose of 15mg/kg is recommended as it may reduce extravascular lung water and leukocyte activation and transfer from donor to recipient.

Duration of physiological optimisation

Emerging data from the United States suggest that prolonged organ donor management (>20 hours (Christmas et al. 2012)) both increases the number of organs that are retrievable and improves early graft function. If further data confirm this finding, then continuing physiological optimisation for extended periods will need to become the standard of care. This clearly has resource implications, but may also benefit recipients.

Future Innovations

A number of other areas may add further improvements to the above care package in the near future. Remote ischaemic preconditioning, innovative organ preservation solutions and extracorporeal pulsatile perfusion are all currently under active investigation (Dikdan et al. 2012). ■

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24th EAHM Congress
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LUXEMBOURG 2013

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- Presidential dinner for sponsors

Thursday, 28 November 2013

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The official speakers and the keynote speaker "Patient Value in Hospital Management"
(10.30 - 12.30)

GOLDEN HELIX AWARD
(13.30 - 14.00)

STRATEGIC GUIDELINES IN CRISIS
(MERGERS, JOINT VENTURES, OUTSOURCING, HUMAN RESOURCE MANAGEMENT, FINANCIAL RESOURCES)
- Two 30-minute lectures (14.00 - 15.00)
- Poster Session - presentation (15.00 - 15.30)
- Break (15.30 - 16.00)
- Two 30-minute lectures (16.00 - 17.00)
- 45-minute roundtable (17.00 - 17.45)

RECEPTION HOSTED BY THE CITY OF LUXEMBOURG
(Evening)

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(LEAN MANAGEMENT, PURCHASING, USE OF IT)
- Two 30-minute lectures (09.00 - 10.00)
- Break (10.00 - 10.30)
- Two 30-minute lectures (10.30 - 11.30)
- 45-minute roundtable (11.30 - 12.15)

NEW BUILDINGS, NEW LOGISTICS, NEW TECHNOLOGIES
- Two 30-minute lectures (14.00 - 15.00)
- Poster Session: awards ceremony (15.00 - 15.15)
- Break (15.15 - 15.45)
- Two 30-minute lectures (15.45 - 16.45)
- 45-minute roundtable (16.45 - 17.30)

GALA DINNER AT CASINO 2000, Mondorf-les-Bains (L)
(Evening)

INFORMATION

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All presentations will be simultaneously interpreted into English/German/French.

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THE ETHICS OF UNCONTROLLED ORGAN DONATION. UNCONTROLLED ORGAN DONATION IS ETHICALLY NEUTRAL

David Crippen, *MD, FCCM*

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With a shortage of donor organs worldwide, measures are needed to improve rates of organ donation. In this paper Prof. David Crippen proposes that preserving organs for organ donation early on while awaiting consent is ethically neutral and reasonable. Prof. Leslie Whetstine argues that uncontrolled donation after circulatory determination of death is ethically and medically specious.

The benefits of organ donation for the purposes of transplantation are many. The media frequently assures us that some worthy person is always awaiting a potentially donated organ. In the USA there are over 100,000 candidates on the waiting list for various organs and 75 people receive organs daily. 19 people die each day waiting for organs. One organ donor can save up to eight lives (National Network of Organ Donors).

One of the fundamental problems in the organ donation pipeline is the fact that potentially viable organs must frequently repose on various life support systems for prolonged periods during the ethical journey to assure the "dead donor" rule (patient must be dead according to the irreversibility rule) is followed to the letter. The longer organs so repose, the less viable they are at the end of this journey.

> *"The intent to re-start circulation in "uncontrolled" donors is only to maintain organ viability, not to actually "resuscitate" the patient"*

"Uncontrolled" organ donation hastens this process by preserving organs earlier in the game, assuring a bigger supply to meet the demand. This early preservation can be by initiating early CPR, extra-corporeal membrane oxygenation (ECMO) and hypothermia protocols on patients deemed otherwise unsalvageable but not technically irreversibly dead (yet). Consent for donation would be awaited expectantly.

This plan seems ethically reasonable if measures are taken to assure an otherwise moribund patient does not become in some sense more salvageable during the process of organ preservation. There are mechanical modes that would spare the brain from any other organ system resuscitation (Wall et al. 2011).

The intent to re-start circulation in "uncontrolled" donors is only to maintain organ viability, not to actually "resuscitate" the patient. If not technically "dead" by rules set forth long before the advent of modern organ system failure reversal, then these potential donors are beyond harm. All the ethical vectors point toward benefit (Glannon 2013).

The "Dead Donor" rule essentially states that patients may not be intentionally killed to get organs. Therefore, clinicians may not hasten this process (kill the patient by some therapeutic manoeuvre) (Truog and Miller 2008). But the majority of deaths in ICUs now involve planned removal of mechanical ventilation (by consent). The clinical reality is that the actions of physicians to allow patients to die as a direct consequence of their fatal disease still, in the end, result in death. Physicians removing mechanical ventilation directly results in cessation of vital function exactly like they might by turning off a car's ignition key or turning off a light switch. The end result is directly affected by an action. A fine line, close to, but perceptible from euthanasia.

If it's ethically acceptable for physicians to actively remove machines that sustain viability, thereby resulting in death with consent, then why is it not equally ethically acceptable to cause death by removing donor organs sustained only by artificial means? (Miller and Truog 2008) If consent is authoritative for organ donation, then why not for pre-morbid procedures that facilitate donation of viable organs?

No patient would die who would not otherwise die. The wishes of patients and surrogates would be honoured more fully and quickly. More viable organs would be made available and the ethics of organ donation would not rest on outdated definitions of death created before the advent of our ability to reverse organ failure. ■

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THE ETHICS OF UNCONTROLLED ORGAN DONATION. UNCONTROLLED DONATION AFTER CIRCULATORY DETERMINATION OF DEATH IS ETHICALLY PROBLEMATIC

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In a typical Uncontrolled Donation After Circulatory Determination of Death (DCDD) case, a patient is brought to the Emergency Department suffering a cardiac arrest, and all resuscitation techniques are initiated in order to save the individual's life. When resuscitation fails, death is declared using the circulatory criterion and the Organ Procurement Organization (OPO) is notified. Donor status is then confirmed via a registry, and a 2-5 minute no-touch interval elapses to be sure that the patient will not auto resuscitate (AR). After these criteria are met organs are procured as rapidly as possible. In some cases extra corporeal membrane oxygenation (ECMO) is used to restart circulation in order to protect organs from ischaemic injury and enhance post transplant viability.

Once circulation stops the shortest time period from a declaration of death to procurement is required to avoid damage to the organs. The primary question is: can we rely on the circulatory criterion alone to determine death when the need for speed is paramount, and still maintain the integrity of the dead donor rule (DDR)?

I argue that Uncontrolled DCDD donors may not be dead - yet. First, AR hasn't been sufficiently studied in this patient population to conclude that it won't occur during the 2-5 minute no-touch interval. Second, cessation of circulation prognosticates death, but it is not sufficient to diagnose death without a neurologic exam in this context. Third, and most troubling, is the use of ECMO in these donors, which restarts circulation thereby nullifying the criterion of death it relied on to determine death in the first place.

AR occurs when circulation spontaneously returns after a period of circulatory arrest. Removing organs during the time in which AR is possible would mean circulation had not been irreversibly lost and the patient may have been dying, but was not dead. Removal of organs during this time would be a clear violation of the DDR and akin to murder. AR is a poorly understood phenomenon that is more likely to occur after resuscitation has been initiated, making this a particular concern for Uncontrolled DCDD. It has been hypothesised that AR may occur as a delayed response to the medications given during Advanced Cardiac Life Support protocols.

The literature on AR is sparse and consists primarily of case reports. A 2010 study indicates that the variability of AR, which has occurred up to 33 minutes after cessation of CPR, means that prospective studies are needed before any specific time interval can be endorsed (Hornby et al. 2010). Given the lack of data, the no-touch period of 2-5 minutes following cessation of CPR would likely be insufficient to rule out this phenomenon, which means that the patient may be dying but is not yet dead.

> *"AR is a poorly understood phenomenon that is more likely to occur after resuscitation has been initiated"*

Another serious objection to Uncontrolled DCDD is that it relies solely on the circulatory criterion to determine death without regard for neurologic status. Heart and lung function are relevant only in that their prolonged absence will lead to a dead brain. Only total brain failure is both necessary and sufficient to determine death. Cessation of circulation is sufficient (but not necessary) for death to be declared. This demonstrates that it is brain function, not circulation itself that distinguishes life from death, since continued circulation does not obviate a determination of death but continued neurologic function clearly does.

Further, one might wonder why clinicians would ever bother to start resuscitation on a patient if the absence of circulation makes one instantly dead. There is a continuum on which one can be dying versus dead. DCDD claims to be able to locate an exact moment of death, a disingenuous claim at best and potentially lethal at worst.

Proponents of DCDD will point out that according to the Uniform Determination of Death Act (UDDA) (National Conference of Commissioners on Uniform State Laws 1980) death can be declared using either circulatory or neurologic criteria. However, the UDDA was established over 30 years

ago when bifurcating death for the purposes of expediting organ transplants was not considered. Nonetheless, supporters of Uncontrolled DCDD who appeal to this argument will have to either conclude that a person is irreversibly dead 2-5 minutes after circulation has ceased (despite the overwhelming data on resuscitation that shows otherwise), or accept that death can be declared even if the brain may still be functional.

> *"The only time circulation can continue and death can be declared is when the patient is determined dead on neurologic criteria"*

Finally, and most pernicious, is the use of ECMO in these patients. In order to avoid cardiac or brain perfusion, a balloon catheter to occlude the thoracic aorta is used (Magliocca et al. 2005). This practice indicates that the transplant team clearly understands that circulation has not been irreversibly lost and that brain perfusion and subsequent reanimation is possible, again reinforcing the problem that such patients are dying but not dead. If circulation is restored, the patient, by definition, has not irreversibly lost circulatory function and could only legitimately be pronounced dead using neurological criteria. The only time circulation can continue and death can be declared is when the patient is determined dead on neurologic criteria.

In conclusion, Uncontrolled DCDD is ethically and medically specious for three reasons:

1. The prospect of AR has not been sufficiently studied to determine that it will not occur in this population of patients, which means dying patients may be mistaken for dead patients;
2. It relies solely on the circulatory criterion, independent of brain status to declare death;
3. By restarting circulation but preventing brain perfusion, it contravenes the criterion used to determine death and clearly acknowledges that brain function may not have been irreversibly lost.

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RESPIRATORY MONITORING IN THE PERIOPERATIVE PERIOD

A recent large prospective cohort study conducted on different types of surgery has demonstrated that the incidence of in-hospital mortality and postoperative pulmonary complications (PPCs) is relatively high. Moreover, PPCs are associated with prolonged hospital stay and higher hospital mortality (Pearse et al. 2012). Ongoing studies are trying to find effective strategies for improving outcome. A keystone in PPCs prevention and early treatment is intensive perioperative respiratory monitoring. In this review, the authors aim to describe different methods to monitor respiratory function during the perioperative period in general and under specific conditions, and the role of recently published predictive scores.

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Respiratory Function During the Perioperative Period

The induction of anaesthesia and curarisation lead to a loss of normal coordination of respiratory muscles, reduction of diaphragmatic tone, decrease in functional residual capacity (FRC), oxygen reabsorption and changes in surfactant function. These factors are associated with the formation of atelectasis, collapse of small airways and decrease in respiratory system compliance. Atelectasis leads to deterioration of ventilation/perfusion ratio and increase of intrapulmonary shunt. Furthermore, the absence of positive end-expiratory pressure (PEEP), the use of high tidal volume ventilation and high plateau pressure (>10 ml/kg and >30 cmH2O, respectively) are associated with the occurrence of Acute Respiratory Distress Syndrome (ARDS) (Tusman et al. 2012). Pathogenesis of perioperative ARDS involves tidal recruitment and cyclic opening and closing of the boundary between aerated and collapsed lung units, and tidal over-distension in non-atelectasis lung units (Slinger 2008).

Basic Tools for Monitoring

Since early detection is essential for prevention and for delivery of appropriate treatment, such as non-invasive ventilation in atelectasis or adequate PEEP during general anaesthesia, integration of various monitoring tools is warranted. In a cohort of 2,000 reported incidents during general anaesthesia, simple pulse oximetry or capnography could detect over half of all events (Webb et al. 1993).

Pulse Oximetry

For prediction of PPCs, a large prospective cohort study in 2,464 patients undergoing surgical procedures by the ARISCAT group has shown that 28.6% of patients with SpO2≤ 90% developed at least one post-operative in-hospital pulmonary complication, therefore preoperative SpO2 has been included in the ARISCAT PPCs prediction score (Canet et al. 2010). In perioperative and recovery rooms, pulse oximetry plays a role in detection of hypoxaemia and related events, without affecting mortality (Moller et al. 1993; Pedersen et al. 2009). A recent study showed that pulse oximetry surveillance reduced rescue events and intensive care unit transfers (Taenzer et al. 2010).

Since SpO2 is physiologically related to PaO2, according to the oxyhaemoglobin dissociation curve, in patients with PaO2 higher than 60 mmHg, SpO2 has low sensitivity for detection of hypoxemia. However a study in ARDS patients has demonstrated a good correlation between SpO2/FiO2 ratio and PaO2/FiO2 ratio and proposed its use in substitution of PaO2/FiO2 ratio (Rice et al. 2007).

In the emergency room pulse oximetry can underestimate

> *"Respiratory monitoring is essential in the perioperative period to optimise mechanical ventilation, for risk stratification and for early detection of postoperative pulmonary complications"*

oxygenation in patients with septicaemia and septic shock (Wilson et al. 2010). Nail polish, especially white, black, purple and dark blue can affect the measurement of SpO_2 although the range of error is ±2% (Hinkelbein et al. 2007).

Capnography

The capnogram is a simple non-invasive method for the assessment of blood CO_2, and can reflect alveolar ventilation, pulmonary perfusion and appropriate connection of ventilatory apparatus to the patient. The waveform characteristics of capnography comprise three phases (see Figure 1). Phase I, which is breathed out initially, represents the dead space due to airway anatomy and apparatus. Phase II represents the alveolar gas emptying from alveoli. Phase III represents CO_2 removal from alveolar gas. The end-tidal CO_2 concentration ($PetCO_2$) is measured at the highest point in phase III. This parameter is an indirect measurement of $PaCO_2$. Figure 1 also shows common pathological findings in capnography.

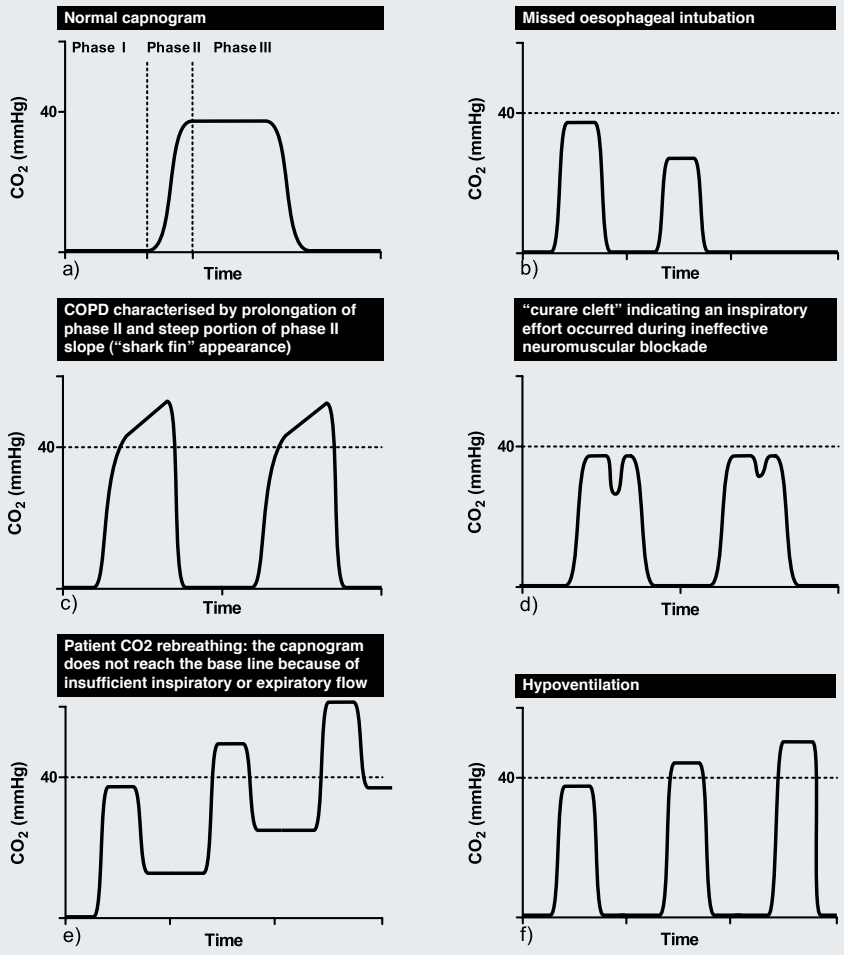
Other Tools

Current evidence supports the potential role of protective low tidal volume ventilation in healthy lungs during general anaesthesia in decreasing the incidence of PPCs (Pelosi et al. 2011; Moriondo et al. 2012; Serpa Neto et al. 2012; Hemmes et al. 2013). The role of PEEP level is still controversial. However, data from large randomised controlled trials should be available soon (Hemmes et al. 2011). Ongoing large prospective observational and randomised controlled studies will provide further information (University Hospital, Clermont-Ferrand ; Hemmes et al. 2013).

Respiratory Mechanics

In the intraoperative period, the airway pressure and compliance measurement could be helpful to optimise the appropriate tidal volume, plateau pressure and PEEP. In some circumstances, such as postoperative intra-abdominal surgery, obesity and patients with increased intra-abdominal pressure (IAP), respiratory compliance is not only affected by lungs but also by the chest wall, and the airway pressure might not represent the real stress-and-strain of the lungs. Preoperative oesophageal catheter placement can measure transpulmonary pressure (Ptp), work of breathing and intrinsic PEEP in high-risk patients. Ptp is the distending force of the lung and is the difference between Palv and Ppl where Palv is the alveolar pressure and Ppl is the intrapleural pressure, measured by balloon placement in the oesophagus. Thus, the measurement of oesophageal pressure could be of help for better titration and optimisation of the pressure required for alveolar recruitment, the tidal volume, and safe plateau pressure as well as the PEEP level during the perioperative period (Pelosi et al. 2011). Furthermore, oesophageal pressure monitoring can be used in the post-operative period to minimise patient-ventilator asynchronies, particularly in COPD patients.

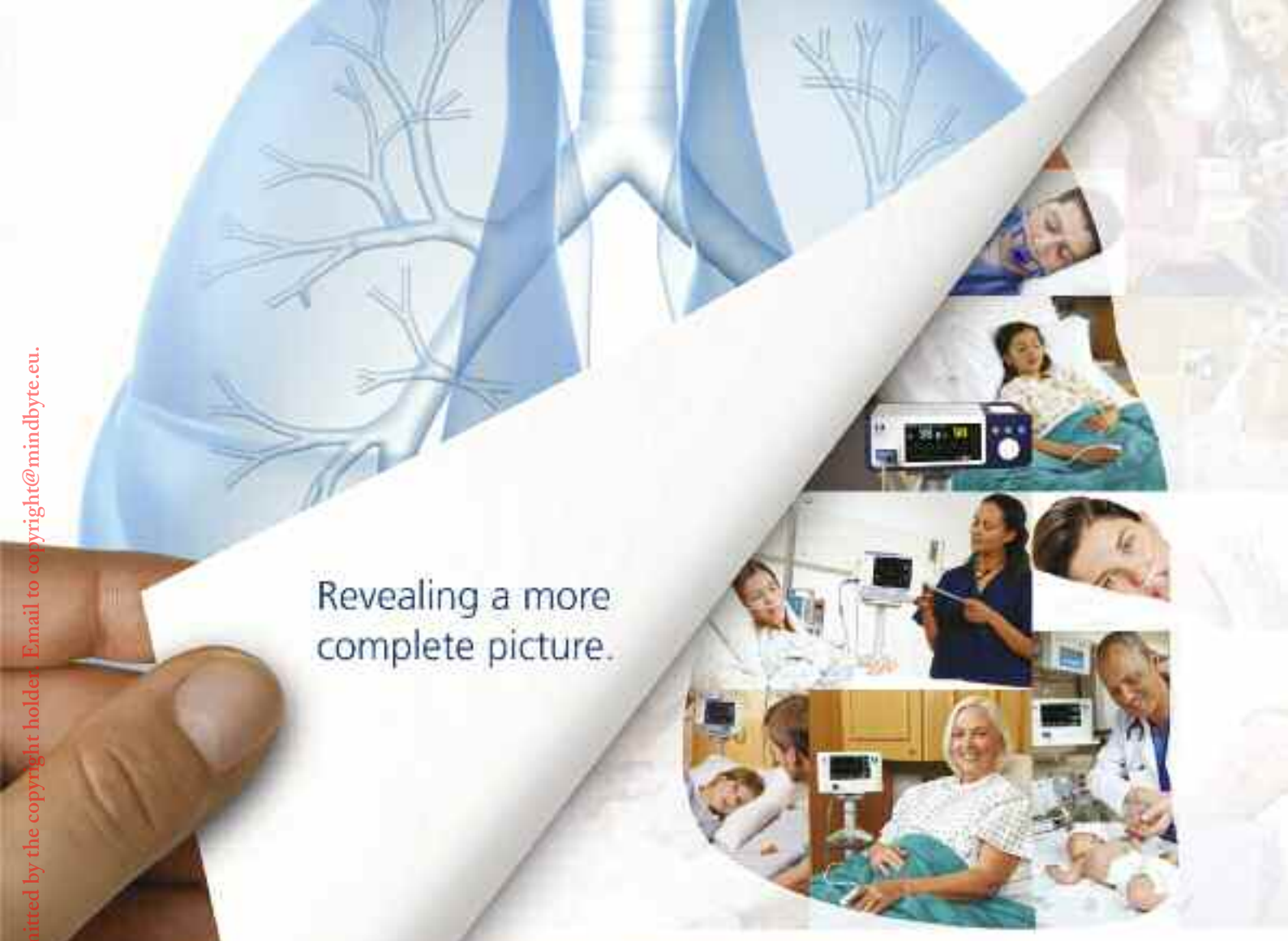
Figure 1. Figure 1 illustrates different capnograms.



Haemodynamics and Respiration

The emergence of new mini-invasive techniques for haemodynamic assessment allows continuous monitoring of cardiac output and other parameters at the bedside, giving prompt information about the role of haemodynamics in the development of respiratory failure. Many of these methods are based on pulse pattern analysis, which can be measured even on a peripheral arterial line, during or after major surgery (Jones et al. 2006; Cannesson et al. 2009). Recently a totally non-invasive alternative has been proposed, but its accuracy is under debate (Broch et al. 2013). Minimally invasive techniques allow transpulmonary thermodilution to estimate extravascular lung water (EVLW) and EVLW index (EVLWi) (Michard 2007). Transthoracic echocardiography has been proposed for estimation of cardiac output (Demirkol et al. 2013). The above-mentioned techniques allow the evaluation of stroke volume variation, which is of emerging interest in the evaluation of patient fluid responsiveness (Cannesson et al. 2009).

Most studies conclude that haemodynamic goal-directed therapy can improve outcome in high-risk surgical patients (Vincent et al. 2012),



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especially in terms of reduction of post-operative complications, while mortality reduction is significant only in very high-risk surgical patients (Cecconi et al. 2013).

Ultrasonography and Respiration

There is emerging consensus about the possibility of using bedside lung ultrasound (LUS) for respiratory monitoring (Bellani et al. 2012; Luecke et al. 2012; Via et al. 2012), for the early assessment of PPCs such as pneumothorax (Ueda et al. 2011), and to monitor the response to non-invasive ventilation (Liteplo et al. 2010) and pharmacological therapy (Via et al. 2010). LUS is capable of estimating EVLW non-invasively at the bedside (Baldi et al. 2013) (see Figure 2). Computer-aided quantification of LUS has been recently proposed (Corradi et al. 2013), and could lead to a reduction in time-consumption and operator-dependence.

Figure 2. Lung ultrasonography showing multiple coalescent B-lines arising from the pleural line (blue arrows), a hallmark of presence of extravascular lung water

Monitoring in Specific Conditions

Obesity, Obstructive Sleep Apnoea

In morbid obesity the forced vital capacity, maximal voluntary ventilation and expiratory reserve volume are markedly reduced. During anaesthesia, an increase in BMI has a good correlation with a decrease in lung volume, lung compliance and oxygenation (Pelosi et al. 1998) and with increase of lung resistance. The decrease of functional residual capacity is linked with atelectasis formation. (Pelosi et al. 2010). Ventilator settings during anaesthesia in obesity should include: 1) low tidal volume ventilation 2) open lung approach by PEEP and recruitment manoeuvre 3) FiO2 less than 0.8 (Pelosi et al. 2010). We recommend monitoring carefully airway plateau pressure, intrinsic PEEP and Ptp. Further studies are warranted to define the optimal respiratory monitoring and setting in this group of patients.

In patients with obstructive sleep apnoea undergoing elective surgery, an oxygen desaturation index ≥ 5 is associated with higher incidence of PPCs (Hwang et al. 2008). Thus, in patients with high sleep apnoea clinical scores should be closely monitored for oxygenation during the perioperative period (Gali et al. 2009). In a recent large cohort study determining the impact of sleep-disordered breathing (SDB) on postoperative outcome in patients undergoing elective surgery, despite an association of SDB with postoperative cardiopulmonary complications, the diagnosis of SDB was not independently associated with increased in-hospital mortality (Mokhlesi et al. 2013).

Role of Recently Published Predictive Scores

Risk factors associated with PPCs depend on basic underlying status, method of anaesthesia, smoking status, type of surgery and postoperative anaesthetic drugs. The type of surgeries most closely associated with PPCs are abdominal aortic aneurism repair, oesophagectomy and major abdominal surgery (22.5, 18.9 and 14.2% respectively) (Smetana et al. 2006). Several investigators demonstrated that the overall risk of PPCs can be predicted, and developed different scores. Most of the parameters needed for score calculation can be assessed at the bedside, and these scores can help physicians to identify high-risk patients who require intensive monitoring (see Table 1).

Investigators from the Veterans Health Administration combined several factors to develop a postoperative respiratory failure risk index (PRF) and pneumonia risk index, already validated, for postoperative respiratory failure in major non-cardiac surgery based on National Surgical Quality Improvement Program (NSQIP) data. These indexes have some limitations in terms of generalisability because the majority of the population were male veterans (Arozullah et al. 2000; Arozullah et al. 2001), and the inclusion of numerous risk factors in the index makes it difficult to use in everyday clinical practice. These indexes were included in a systematic review (Smetana and Lawrence 2006) and

Table 1. Predictive Scores

Score	PRF	Postoperative pneumonia risk index	Postoperative pulmonary complications risk score	SLIP	UEPI index	Postoperative respiratory failure risk calculator	SPORC
Authors	(Arozullah et al. 2000)	(Arozullah et al. 2001)	(Canet et al. (2010)	(Kor et al. 2011)	(Ramachandran et al. 2011)	(Gupta et al. 2011)	(Brueckmann et al. 2013)
Population	181,109 Male veterans	316,071 Mainly male veterans	2,464	4,366	331,664	468,795	29,924
Incidence of PPCs	3.4%	1.5%	5%	2.6%	0.83–0.9%	3.1%	0.41%
Type of surgery	Non cardiac surgery	Non cardiac surgery	Non obstetric surgery	Major surgery, mechanical ventilation > 3 hours	Non cardiac , non-emergency surgery	All	General anaesthesia
Risk factors	Emergency surgery Age Functional status COPD	Emergency surgery Age Functional status Weight loss COPD General anaesthesia Impaired sensorium Stroke Transfusion Long-term steroid use Smoking Alcohol abuse	Age Recent respiratory infection Type of surgery Surgical incision Duration of surgery Emergency surgery	Diabetes COPD GERD Alcohol abuse -	BMI Alcohol abuse Current smoker Dyspnoea COPD Diabetes CHF HT Cancer Prolonged hospitalization Weight loss Sepsis	Surgical procedure Emergency surgery ASA Functional status Preoperative sepsis	ASA score Emergency procedures High-risk service CHF COPD
Laboratory tests	Albumin Blood urea nitrogen(Bun)	Bun	Pre-operative SpO2 Pre-operative Hb <10 g/dL		Liver function	-	-

in the 2006 American College of Physicians guideline (Qaseem et al. 2006).

Canet et al., for the ARISCAT group, have recently identified variables, namely pre-operative arterial oxygen saturation, pre-operative haemoglobin concentration (less than 10 g/dL) and respiratory infection in the previous month, as strong predictors. Additionally, the study has confirmed that surgical procedure and duration are predictors of PPCs. The areas under ROC curve are 90 and 80 for the development of PPCs predictive index and the validation of this index, respectively. The promising advantages of this score are simple clinical assessment and use of objective variables. A large European study (PERISCOPE) has been completed, and will act as external validation of this score (Canet et al. 2011).

Kor et al. developed the surgical lung injury prediction score (the SLIP score) for distinguishing patients undergoing high-risk surgery WHO will need mechanical ventilation during general anaesthesia for longer than three hours and for predicting the occurrence of postoperative ARDS. This score can identify patients that will develop early postoperative ARDS with an AUC of 0.82 (95% CI 0.78-0.86) (Kor et al. 2011). However, this study could be biased by its single centre retrospective design and heterogeneity of population.

Based on ACS-NSQIP data, on 222,094 patients, Ramachandran et al. developed the unanticipated early postoperative intubation risk class index (UEPI index), suggesting that close respiratory monitoring during non-invasive ventilation after abdominal surgery might reduce tracheal intubation in high risk patients (Ramachandran et al. 2011). Additionally, Gupta et al. developed the postoperative respiratory failure (PRF) risk calculator based on a logistic regression model. PRF risk calculator is available online and as a mobile application designed for physicians (Gupta et al. 2011). Bruekmann et al. reported the Score for Prediction of Postoperative Respiratory Complications (SPORC), focusing on the early re-intubation within three days after surgery as primary endpoint, with an AUC of 0.81 that can be easily used preoperatively by anaesthesiologists (Brueckmann et al. 2013).

Conclusion

Respiratory monitoring is essential in the perioperative period to optimise mechanical ventilation, for risk stratification and for early detection of postoperative pulmonary complications. A deep knowledge of different monitoring techniques is crucial to improve the quality of care in surgical patients. ■

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Nihon Kohden is redefining Quality of Care with new, non-invasive technologies like Pulse Wave Transit Time (PWTT) and Estimated Continuous Cardiac Output (esCCO) by introducing volumetric information to all care levels. esCCO is a new technology to determine the cardiac output using pulse wave transit time. PWTT requires only the pulse oximetry and ECG-signals from each cycle of the ECG. esCCO provides real-time, continuous and non-invasive cardiac output measurements.

Principle of esCCO

The formula providing cardiac output values is determined by expressing the PWTT information as follows:
$CO = SV \times HR = K \times (\alpha \times PWTT + \beta) \times HR = esCCO$[1]

PWTT is the time measured from the peak of the ECG R-wave to the pulse wave rise point, representing the time for the pulse wave to reach the peripheral vessel. (Fig.1). PWTT has been shown to be well correlated with stroke volume, and this relationship is used to calculate esCCO[1].

Performance of esCCO

Ishihara et al. reported that esCCO is highly correlated with cardiac output as measured by the thermodilution technique[2]. In 2009, a multi-center study involving seven facilities verified the effectiveness of esCCO as a practical application[3] (Fig.2).

Reliable Measurement with Non-Invasive Calibration

By only entering patient information including age, gender, height and weight, and performing an initial NIBP measurement, esCCO determines a reference value for calibration and the measurement is ready to start. Additionally, a cardiac output value obtained by other CO devices such as by pulmonary artery catheter can be used for calibration. Both calibration modes reliably track changes in cardiac output and provide advanced monitoring and trending of the patient's hemodynamic status.

Case Report

Comparison of trend performance of esCCO and APCO in kidney transplantation

Introduction

Perioperative goal directed therapy (GDT) based on measurement of stroke volume (SV) is expected to improve postoperative outcome[4]. A device that can accurately measure stroke volume (SV) during surgery and is both minimally-invasive and low cost is ideal. Many methods have been developed as less-invasive and continuous measures of SV; the Pulse Contour and Intrathoracic Impedance methods have been widely used in clinical practice.

Estimated continuous cardiac output (esCCO) is a technology that continuously and non-invasively measures SV based on pulse wave transit time (PWTT) by using only information derived from electrocardiogram (ECG), pulse oximeter (SpO2) and

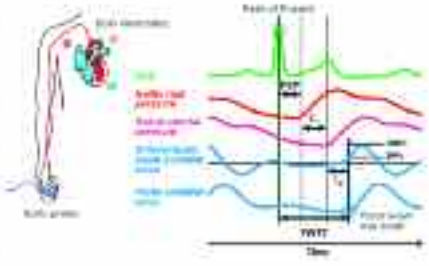

Figure 1. Pulse wave transit time (PWTT) derived from ECG and pulse oximetry signal. PWTT consists of 3 time components: pre-ejection period (PEP), the time for the pulse wave to travel through large elastic and muscular arteries, (T1), and the time for the pulse wave to travel through peripheral arteries (T2).

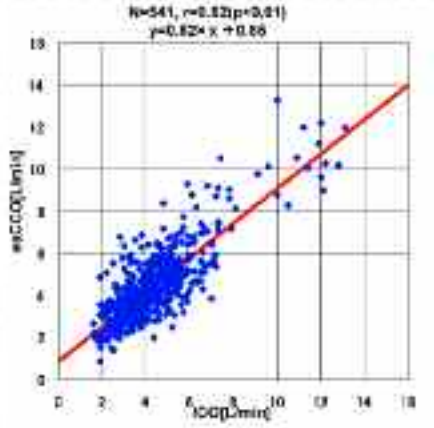

Figure 2. Comparison between esCCO and cardiac output by cold bolus thermodilution (ICO).

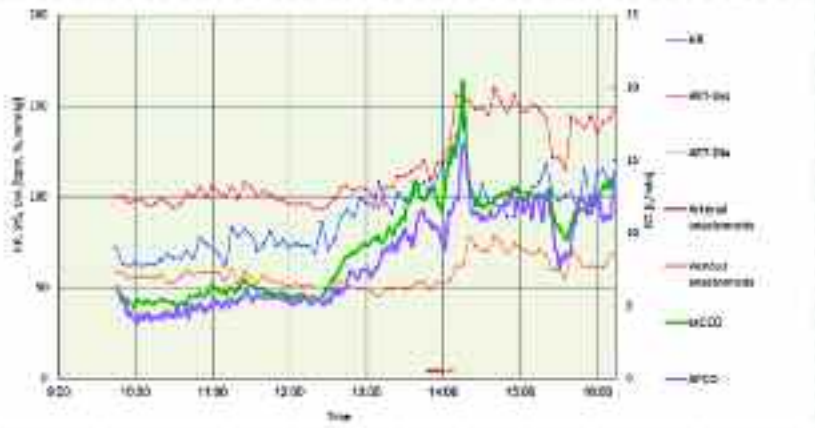

Figure 3. Trendgraph of APCO and esCCO in kidney transplantation. esCCO is in good agreement with APCO throughout the surgery.).

blood pressure[3]. We evaluated the performance of esCCO to trend changes in SV as compared to arterial pressure-based cardiac output (APCO) in kidney transplantation. One of the cases is presented here.

Materials and methods

Patients scheduled for kidney transplantation and able to provide informed consent were enrolled. In this case, a 36 year old male (182cm, 90.5kg) was evaluated. The surgery was performed under general anesthesia. Anesthesia was induced with fentanyl citrate, midazolam, and rocuronium bromide and maintained with continuous infusion of sevoflurane (1.0-2.0%) and remifentanil hydrochloride (0.05-0.5 mcg/kg/min). In addition to measurements of ECG, SpO2 by pulse oximetry, rectal temperature, and end-tidal carbon dioxide (etCO2), radial artery and central venous catheters were inserted after the induction of anesthesia.

Results

APCO was 5.3L/min and esCCO 5.2L/min at the start of the surgery. Cardiac output (CO) was increased after fluid challenge. APCO and esCCO, at the end of arterial anastomosis, were significantly increased to 16.0L/min and 20.2L/min, respectively. The measured esCCO showed strong agreement with APCO throughout the surgery.

Discussion

Perioperative fluid optimization based on SV can lead to reduced hospital stay, reduced chance of postoperative nausea and vomiting (PONV) and associated complications, with faster postoperative recovery of gastrointestinal function[4].

In Japan, APCO is widely used to monitor SV during surgeries because: 1) the accuracy of APCO has been shown to be clinically acceptable[5], 2) it is less-invasive, and 3) it is easy to use.

In this case report, we compared APCO and esCCO during kidney transplantation in a patient where hemodynamics changed significantly. This case shows the performance of esCCO to track changes in cardiac output when compared to APCO (Fig.3).

The Pulse Contour and Impedance methods are well established as less-invasive measurements of SV, and APCO is especially popular. APCO is based on the pulse contour analysis, and the principle of esCCO is based on PWTT. While APCO requires radial artery catheterization, esCCO can be non-invasively measured only by measuring ECG, SpO2 and blood pressures without additional sensors. Perioperative SV monitoring is believed to improve the quality of care in patients undergoing surgery; esCCO can provide flow-related parameters such as SV and CO derived by routinely measured parameters and be useful to guide intraoperative goal directed fluid therapy.

To establish the clinical benefits of esCCO, evaluations of esCCO continue, globally, with added emphasis on the fluid responsiveness of esCCO in GDT protocols.

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INTELLIGENT VENTILATION IN THE ICU
TECHNOLOGY IMPROVING PATIENT OUTCOMES

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Intelligent ventilation is the appropriate application of a suitable mode of ventilation in each clinical situation with online, automated adjustment of the mode and level of support when the patient's respiratory needs alter and with automated weaning as soon as possible to reduce the time of mechanical ventilatory support and days in the ICU.

Using intelligent ventilator technology most patients can be automatically ventilated (optimally) according to the least work of breathing fit of the measured mechanics of the lungs and chest wall. Simply by providing the maximal alveolar ventilation for the lowest needed minute ventilation, and therefore the least dead space ventilation, the resulting blood gases are likely to be the best possible for the state of the lungs. In addition, the importance of preventing the development of intrinsic positive end expiratory pressure (Auto PEEP) while maximising alveolar ventilation, particularly in patients with obstructed airways, was recognised. Thus, the initial development of adaptive support ventilation (ASV) machines without the need for end tidal CO_2 feedback in the closed loop, proved the reality of the least work of breathing philosophy in the optimal mechanics of ventilation of most patients.

Further development of the Intellivent™ (Hamilton Medical, Bonaduz, Switzerland) closed loop system, using online capnography and pulse oximetry with artifact elimination, has extended the capability of intelligent ventilation to include automating the minute ventilation target as well as the FiO_2 and PEEP settings.

Our clinical experience with these forms of intelligent ventilation is that we shorten patient ventilation days, reduce morbidity associated with mechanical ventilation and generally improve patient outcomes. An added benefit that we notice on a daily basis is a dramatic reduction in medical and nursing staff workload as intelligent ventilation eliminates the need, hour by hour, to make changes to ventilator settings to apply weaning protocols.

Introduction

Pressure support ventilation (PSV) is the most well-known, basic and effective form of closed loop control ventilation and is widely used today. The clinician sets a target pressure (the pressure support setting), and flow (the output) is automatically adjusted to maintain that pressure throughout inspiration. The ventilator monitors airway pressure (the target), and the control algorithm continuously modulates the flow (the output) to achieve the desired pressure. Patients are usually most comfortable on this simple form of closed loop support. However, the amount of pressure support (the PS target) needs to be constantly updated and, when weaning is desired, gradually reduced by the clinician hour by hour.

The basis of intelligent ventilation is the application of the closed loop automated algorithm of the adaptive support ventilation (ASV) technology, which uses a number of different modes, including PSV and pressure controlled synchronised intermittent mandatory ventilation (SIMV) as needed by the patient, (Mireles-Cabodevila et al. 2009; Conti and Costa 2010). ASV intelligently and automatically adapts the respiratory rate and level of ventilatory pressure to the patients' passive and active respiratory mechanics (Branson 2000; Campbell et al. 2001; Tassaux et al. 2002). ASV warrants that the pre-determined target minute ventilation, based on ideal body weight and percent minute volume settings, is delivered to the patient.

Using online, breath-by-breath analysis of lung function, the ventilator is driven by a programmed computer to provide optimal alveolar ventilation, according to the patient's changing requirements (Linton 2001; Brunner and Iotti 2002). The programming is based on a concept of maximal energetic benefit: at any single breath the ventilator selects the respiratory rate target (and hence the tidal volume target) that corresponds to the minimal work of breathing of the patient-ventilator unit.

The automatic selection of targets is based on data for series dead space and expiratory time constant, which are provided by a lung function analyser that is communicating continuously with the ventilator's controller. The lung function analyser also calculates compliance, resistance and air trapping (residual end expiratory flow), in order to optimise respiratory flow patterns and the inspiration: expiration ratio. Target volume and rate are calculated specifically for each patient

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INTELLiVENT®-ASV: the first Ventilation Autopilot

As a clinician, you define the ventilation strategy and set the targets for your patient's oxygen saturation and $etCO_2$ levels. INTELLiVENT-ASV then **automatically adjusts the ventilation parameters depending on the patient's condition and your inputs**, breath by breath – allowing you to **focus on other aspects of patient care**. And, when the patient's condition allows, INTELLiVENT-ASV can even **guide the weaning process**.

INTELLiVENT-ASV is the result of three decades of research and 15 years of clinical use as ASV (Adaptive Support Ventilation). In a recent comparison, it received top ratings for its capabilities related to:

- Safety
- Patient comfort
- Patient liberation from ventilation [1]

And it has been shown[2] that manual can be massively reduced. [2]

www.hamilton-medical.com/intellivent

1 Alonso-Calzadilla, E., Holanda, M. A. & Chatburn, R. L. (2010). A rational framework for selecting modes of ventilation. Respiratory Care, 54(3), 348-356.
2 Lellouche, F., Bouchard, P. A., Simard, S., Chen, E. & Wysocki, M. (2013). Evaluation of fully automated ventilation: a randomized controlled study in post-cardiac surgery patients. Intensive Care Med. 2013 Mar;39(3):463-71.

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Table A. Patient Data

N (%)	Ventilated Cases N=1220
63.1 ± 18.8	Age (yrs) ± SD
Males/Female 60/40	Gender
	Diagnoses
429 (35)	Respiratory
480 (39)	Infectious
234 (19)	Cardiac
238 (20)	Renal
137 (11)	GI & Hepatic
176 (14)	Neurological
96 (8)	Hematological
47 (4)	Metabolic
174 (14)	Other
27.4 ± 9.8 median 27	APACHE II score ±SD
57.2 ± 27.8 median 60	Predicted mortality (%)
9	GCS (median)
	Cause of Death in ICU: N=406
288 (71)	Sepsis and MOF
38 (9)	Respiratory
32 (8)	Cardiac
18 (4)	Anoxic Brain damage

GI – Gastro-Intestinal
APACHE – Acute Physiological and Chronic Health Evaluation
GCS – Glasgow Coma Scale
MOF – Multi-organ failure

in order to achieve the set target minute volume according to the patient's lung mechanics (compliance, resistance, air trapping, dead space and expiratory time constant) and peak airway pressures.

At any breath, the controller compares target and actual data for tidal volume and respiratory rate, and programmes the mandatory rate and inspiratory pressure to be applied in the next breath, to approach the desired targets (Laubscher, Frutiger et al. 1994; Laubscher, Heinrichs et al. 1994; Weiler et al. 1994). Inspired pressures are either delivered using pressure control in apnoeic patients or pressure support in spontaneously breathing patients.

Our Experience with ASV

We recently audited our experience with ASV in our Medical Intensive Care Unit over the past decade (Linton 2012; Sviri et al. 2012) (See Tables A and B). Mean length of ventilation (all modes) was more than 10 days with a median of 6 days. Sedation was required in 812 patients (67%) for a median length of 2 days. Nine hundred and forty eight patients were ventilated with ASV for more than 50% of the time (93%). Sixty-eight (6%) patients required transition from ASV mode to pressure control mode (PCV). The primary indication for switching from ASV to PCV was to satisfy our technical requirement for a stable tidal volume to allow administration of inhaled Nitric Oxide (NO). Respiratory complications included ventilator-associated pneumonia (VAP) in 288 patients (23.6%); pneumothorax developed in less than 1% of all patients ventilated with ASV. Weaning from mechanical ventilation was mostly (86%) performed with ASV.

Table B. Ventilation Data

Mode*	Total Ventilation	Median	Mean ± SD
All Modes (N=1217)	12467	6	10.2 ± 12
ASV (N=1212)	9220	6	9.1± 10.5
SIMV (N=176)	965	3	5.5 ± 5.9
Pressure control (N=124)	628	3	5.1 ± 6.2
Pressure support (N= 131)	662	3	5.05 ± 6.1
ASV > 50% of the time**	948 / 1016 (93%)		
Relative vent days on ASV	9220/1246	74%	
Morbidity Aspects:	7	(13%)	
Tracheostomy needed in ICU	159	(12%)	
Failed Extubations	97/784	(19%)	
Ventilated on discharge to ward	235/1220		

Initiation of Ventilation (N = 1220)
Admitted on Ventilator 931 (76)
Ventilation initiated after admission 289 (24)

ASV requires that an adequate and optimal target minute volume is set according to the ideal body weight (Dongelmans et al. 2008). Few manual manipulations of the ventilator are required (Petter et al. 2003), and the automated controller provides rapid adaptation to changing ventilator needs of ventilated patients (Linton 2001; Lellouche and Brochard 2009). Our unit does not employ respiratory therapists trained in setting ventilators. Such changes are therefore left to the medical staff in the ICU, who are not always available to quickly respond to changing ventilation requirements. The ASV mode reduces the need for manipulation of the ventilator settings as it adjusts automatically to altered lung mechanics and patients' effort, compensating for reduced staffing levels.

Experience of Others Using ASV

Previous studies have tested the efficiency, safety, and adaptability of ASV in various lung diseases and in patients undergoing general anaesthesia, during position changes and transition between two- and one-lung ventilation (Weiler et al. 1994; Weiler et al. 1998; Belliato et al. 2004). Tassaux and colleagues demonstrated improvement in patient-ventilator interaction and reduction in signs of asynchrony with ASV compared with SIMV and PS in patients during early weaning with partial ventilator support (Tassaux et al. 2002). In their study, which reports the use of ASV as the primary mode of ventilation in a mixed ICU (322 patients), Arnal and colleagues found that ASV was used in 98% of invasive ventilation days, and appropriately selected different rate/volume combinations for patients with different types of underlying lung disease, including acute respiratory distress syndrome (ARDS) and chronic obstructive pulmonary disease (COPD) (Arnal et al. 2008).

ASV has been shown to hasten weaning from ventilation compared to other modes (Gruber et al. 2008). It can appropriately decrease ventilator support in patients with chronic respiratory failure who tolerated a conventional weaning trial, suggesting that this mode may facilitate respiratory weaning (Linton et al. 1994). ASV is practicable as a respiratory weaning protocol in post-surgical patients; it may accelerate tracheal extubation and simplify ventilatory management in patients after cardiac surgery (Sulzer et al. 2001; Petter et al. 2003). It has also been shown to be a safe weaning modality as patient demands are adequately met during weaning from ventilation (Linton et al. 1994; Jaber et al. 2009). In our experience ASV is highly suitable for patients with chronic obstructive lung disease and for weaning most patients from ventilatory support. There was only minimal need to convert any patient from ASV to other modalities during the weaning phase.

ASV has been shown to be safe in a model of ARDS, by limiting peak pressures and reducing tidal volumes (Sulemanji et al. 2009). In our own practice we have found that most patients in our database with ARDS tolerated ASV well throughout the required ventilation of their lung disease. However, a minority of patients (6%) required transition to pressure controlled ventilation, due to patient-ventilator asynchrony, severe hypoxia necessitating inhaled NO or a desire by the attending clinicians to provide more inverse ratio ventilation than the ASV controller allowed.

ASV has been the sole mode of ventilation in some chronic care facilities in Israel for several years (Linton et al. 2006), and has been shown to be cost-effective, safe and efficient in ventilating and weaning

patients with chronic respiratory failure. ASV automatically allows weaning of most patients and therefore requires fewer manipulations of the ventilator during the weaning process.

It is important to realise that both the ASV and the Intellivent™ technology have the capacity to 'recognise' the development of excessive autoPEEP and adjust the I:E ratio accordingly in an attempt to limit the autoPEEP and thus prevent the development of tension pneumothorax, which is a feared complication of mechanical ventilation in severe ARDS. There is clearly a difference of international expert opinion on the ideal PEEP to use, and the temporary use of pressure controlled ventilation (PCV) is an acceptable alternative in more heavily sedated and paralysed patients when inhaled NO is used, to optimise patient-ventilator synchrony and oxygenation.

Intellivent

Intellivent-ASV® (Hamilton Medical, Bonaduz, Switzerland) is a recently released development of ASV that automatically adjusts both ventilation and oxygenation parameters (FiO_2 and PEEP) (Arnal et al. 2012). Minute volume is adjusted according to end tidal CO_2 ($ETCO_2$) measured continuously, and oxygenation is adjusted according to SpO_2 measurements. The only parameter that the physician sets is the patient's ideal body weight. It utilises proprietary algorithms to set optimal ventilation parameters and responds to dynamic changes in SpO_2 and $ETCO_2$. The algorithms are calibrated to different disease patterns (such as ARDS, head injury and chronic obstructive lung disease), which the user selects. The range of acceptable settings is also adjustable by the user and adds a level of safety and individuality. This mode of ventilation has been on trial in our ICU over the past year in an in-house, non-funded clinical study. Our preliminary experience has been that the Intellivent™ technology is safe, and seems able to optimise the PEEP level and reduce the FiO_2 faster than we usually do, in a broad range of ICU patients.

Conclusion

ASV is an acceptable mode of ventilation for complicated medical patients in the MICU with a good weaning success rate and low complication rate. In our recent experience with a number of patients with critical ARDS, or severe restrictive lung disease e.g. pneumonitis, interstitial fibrosis and chest stiffness, Intellivent™ appears to be able to optimise the PEEP and bring the FiO_2 down faster than we were doing with ASV.

The online monitoring of FiO_2 and PEEP with automated adjustment to the target minute ventilation in ASV as well as the visual monitoring of heart-lung interaction parameters, as provided for by the Intellivent™ technology, enhances the automated ventilator's capability to monitor the patients. This completely automated system seems to avoid any need for manual changes to the Minute Volume Target Percentage or to the set PEEP and FiO_2 settings. ■

Conflict of interest statement

The authors declare that they have no conflict of interest in the work, preparation and content of this article.

Disclosure

This invited paper includes a review and update of recent publications by the authors.

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IMPLEMENTING THE HELSINKI DECLARATION ON SAFETY IN ANAESTHESIOLOGY IN EUROPE

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Sven Staender (Chairman), on behalf of the EBA/ESA Task Force Patient Safety (Andrew Smith, Guttorm Brattebø, David Whitaker)

The ESA Patient Safety Starter Kit was launched in June at Euroanaesthesia 2013. This article describes the background to the kit and its development. In addition the work of the ESA's Task Force Patient Safety is described and its strategy for implementing the Helsinki Declaration on Patient Safety in Anaesthesiology.

In June 2010 the European Board of Anaesthesiology (EBA), the European Society of Anaesthesiology (ESA) and the National Anaesthesia Societies Committee (NASC) launched the Helsinki Declaration on Patient Safety in Anaesthesiology (Mellin-Olsen et al. 2010). The aims are simple, ambitious and powerful, and represent a shared European opinion about what is worth doing and practical to improve patient safety in anaesthesiology. The declaration recommends practical steps that all anaesthesiologists as well as national anaesthesia societies should adapt for their own practice.

After the initial signing of the Helsinki Declaration by the ESA member state societies the declaration has been signed by industry representatives and patient organisations. Over the last three years, its existence has spread around the world. To date the Helsinki Declaration has been signed or adopted by a variety of countries and societies worldwide, including Latin American countries, Canada, Australia, New Zealand, the United Arab Emirates and the Confederation of the ASEAN Societies of Anesthesiologists, representing Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand and Vietnam. In addition the Declaration has been signed by hundreds of anaesthetists around the world.

ESA and EBA set up a Task Force Patient Safety in order to help distribute the aims of that Declaration. This Task Force consists of four anaesthetists, two representing the EBA (David Whitaker and Guttorm Brattebø) and two representing the ESA (Andrew Smith and Sven Staender). The aims of the Task Force were to create knowledge and resources for patient safety in order to help implement the Helsinki Declaration. A wide variety of activities has been completed by the Task Force over the last three years. Among them are:

- The template for a Departmental Safety report;
- A drug syringe labelling study (with the Universities of Geneva and Berlin) (Wickboldt et al. 2012);
- A book on patient safety in anaesthesia distributed to every participant of the Euroanaesthesia congress 2011 (Best Practice and Research Clinical Anaesthesiology – Hugo Van Aken, Editor: Elsevier Science, 2011) (van Aken et al. 2011);
- A survey on the use of capnography in Europe (presented at Euroanaesthesia 2012);
- A survey on adherence to core contents of the Helsinki Declaration (presented at Euroanaesthesia 2013) and;
- Crisis checklists that should help to manage critical situations in the perioperative setting. These crisis checklists have been developed together with David Borshoff from Perth, Australia, author of *The Anaesthetic Crisis Manual*, which contains similar checklists as well as accompanying explanations (Borshoff 2011).

After compiling the first draft of these checklists a modified Delphi process was started and the content was sent for comment by invited and experienced anaesthesiologists in Europe. The final draft of these checklists was put up for comment on the members' part of the webpage of ESA. These checklists are a compilation of European approaches to various crisis situations in the perioperative setting. Use of such checklists has been proven to be beneficial in a recent study where the authors found that failure to adhere to life-saving processes of care was less common during simulations when checklists were available and the team performed better when the crisis checklists were available than when they were not (Arriaga et al. 2013).

The Patient Safety Kit

This content has now been compiled in a starter kit, which was distributed at Euroanaesthesia 2013. To cater for the multiple aims of the Helsinki Declaration, the safety starter kit contains the following:

- Selected Articles of the publication "Safety in Anaesthesia" (Best Practice and Research Clinical Anaesthesiology);
- An online basic guide on Patient Safety by Charles

Vincent (Vincent 2012);

- A proposed template for an anaesthesia departmental safety report;
- The text of the original Helsinki Declaration;
- Hazard warnings published in countries that alert anaesthesiologists to important adverse events (examples from the UK, Germany and Switzerland);
- Powerpoint presentations plus audio podcasts of essential aspects of patient safety; Topics covered include human limitations in the operating room, introduction to critical incident reporting etc.;
- Powerpoint presentations of WHO (WHO 2013) and ESA for basic lectures on patient safety / risk management, including topics such as medication error, good communication and team work, simulation, engaging with patients and carers, and understanding clinical risk;
- Checklists for emergency management in the operating room, for situations such as those involving newborns, anaphylaxis, hypertension, hypotension etc.;

Table 1. Communication and Distribution of Helsinki Declaration

Responsibility	Level	Action	Result	Working party
Task Force	European	Announcement of strategy in ESA newsletter	Dispersion of Knowledge	Task Force
Task Force	European	Promoting publication of the HD on websites of other European medical scientific societies	Creating support among a broad field	ESA headquarter
Task Force	European	Setting up a strategy to approach the media for articles and interviews	Creating understanding and support in the public	ESA headquarter
Task Force	European	Preparing resources (starter kit)	Creating teaching material	Task Force
National Task Force	National	Announcement in national scientific or society journal	Dispersion of Knowledge	National expert group
National Task Force	National	Article or interview in national public medical journal	Dispersion of Knowledge	National expert group
National Anaesthesia Society	National	Putting the translated Helsinki Declaration on the website	Make declaration accessible for users	Webmaster of national society
National Anaesthesia Society	National	Promoting publication of the HD on websites of other national medical scientific societies	Creating support among a broad field	PR officer national society
National Anaesthesia Society	National	Setting up a strategy to approach the media for articles and interviews	Creating understanding and support in the public (national)	PR officer national society
National Anaesthesia Society	National	Organisation of workshops, e-learning modules using the TF-starter kit	Preparing national implementation of the HD	National expert group
National Anaesthesia Society	National	Setting up quality programmes	Embedding safety in daily practice	Hospital organisations
National Anaesthesia Society	European	Annual report of the degree of national implementation of HD back to EBA/ESA and applying for accreditation	European overview of the implementation of the HD and apply for accrediting national societies that comply with HD	National expert group and Task Force
EBA / ESA board	**European**	**Accrediting national societies**	**HD is implemented and this implementation is visible by the accreditation**	**Task Force**

- The WHO Safe Surgery Checklist; and
- A list of links to important Internet resources.

The starter kit is a collection of necessary resources to help fulfill the aims of the Helsinki Declaration and to make it readily and easily available and useful for anaesthesiologists across Europe and worldwide.

Many of the practices and tools referred to in the starter kit may be commonplace in many hospitals in Europe. But ESA hopes that this starter kit will support hospitals, particularly those in countries that still have a long way to go before the standards of the Helsinki Declaration are fully established.

Next Steps

Following Euroanaesthesia 2013, the ESA will publish the kit in a dedicated section of its website (www.esahq.org), and begin working on implementation of the Helsinki Declaration on a national level. This will be done in collaboration with the EBA, NASC, ESA and the individual national societies.

The survey on the European distribution of the content of the Helsinki Declaration performed by the Task Force Patient Safety, and conducted among the representatives of the national anaesthesia societies (NASC) and the ESA council members, showed that only a few European countries today have implemented all of the content of the declaration. The broad implementation of the content of the Helsinki Declaration will be a major challenge for the future activities of EBA and ESA.

This starter kit will help to provide resources for all interested hospitals, departments of anaesthesiology and national societies. ESA will accompany this process of implementation with a strategy over the next years. This strategy has been worked out with various experienced anaesthesiologists from Europe and approved by the ESA board of directors. It will focus on three major aspects over the next years:

Table 2. Action Required on a European and National as well as Hospital Level

Core recommendation	Aim	Responsibility	Level	Action	Result
Minimum standards of monitoring	Comply with EBA standards	National society	National	Install working party to set up a nationwide enquiry to investigate the current status of monitoring	Overview of shortages in monitoring equipment nationally
	Exploring the current status of monitoring in health care institutions	Head of Dept. of Anaesthesia	Hospital	Bringing the current overview of monitoring devices in the department up to date	Short list of monitoring equipment
	Completing the equipment to comply with standards	Head of Dept. & financial officer of hospital	Hospital	Acquiring funds and defining user specifications for additional equipment	Completion of monitoring status to comply with standard
Availability of Institutional Protocols	Comply with HD list of protocols	National society	National	Setting up a working party to invite national anaesthesia stakeholders to report on the status of safety protocols currently in use in relation to HD	Identification of shortages of protocols nationwide
	To update with standard protocols or to support missing protocols	National society	National	Installing a guideline & protocol committee to ensure availability of updated protocols	A set of protocols for immediate implementation is available
	Comply with published recommendations for available protocols	Head of Departments of Anaesthesiology	Hospital	Implementation of protocols locally	Recommended protocols are available at the workplace
Sedation Standards for safe practice	Exploring the current status of sedation standards	National society	National	Install working party to set up a nationwide enquiry to investigate the current status of sedation practices	Overview of modalities in sedation practice nationally
	Visibility of current recommendations for sedation	National society	National	Publication of established guidelines for sedation practice in national specialists journals/newsletters	Established recommendations are available nationwide
	Comply with established standards	Head of Departments of involved specialties (Radiology, Gastroenterology etc.)	Hospital	Implementation of standards together with the involved specialists	Established standards are implemented on the local level

1. European coordination of activities and resources;
2. National distribution and implementation; and
3. Accreditation of national societies.

Table 1 (p. 31) shows the corresponding activities concerning communication and distribution and Table 2 (above) shows the required action on a European and national as well as hospital level.

What is now required is the support and work of all of us who care for patients every day in the perioperative setting to put the words of the Helsinki Declaration into practice. ■

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INDIRECT CALORIMETRY: RESEARCH TOOL OR ESSENTIAL EQUIPMENT?

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Abbreviations

BEE : Basal Energy Expenditure
BMR : Basal Metabolic Rate
DIT : Diet-induced thermogenesis
EE : Energy Expenditure
FeO_2 : fraction of expired oxygen;
FiO_2 : fraction of inspired oxygen;
IC : Indirect Calorimetry
REE : Resting Energy Expenditure
RMR: Resting Metabolic Rate
RQ : Respiratory Quotient
TEE : Total Energy Expenditure
uN2 : urinary nitrogen component;
VCO2 : production of CO_2;
Ve : Expiratory Volume;
Vi : Inspiratory Volume;
VO_2 : Consumption of O_2

Indirect calorimetry is usually presented as essential equipment to optimise nutrition. However, numerous flaws limit its use, and currently available devices are not sufficiently accurate for clinical use.

Why Use an Indirect Calorimeter in the ICU?

The magnitude of the caloric debt (the difference between energy expenditure (EE) and the caloric intake) has been strongly associated with the rate of complications occurring in ICU patients (Dvir et al. 2006; Faisy et al. 2009; Villet et al. 2005). A large caloric debt is partly explained by the difficulties in providing the desired caloric intake by the enteral route (Artinian et al. 2006). Conversely, a risk of overfeeding (ie caloric intake > EE) is present when EE is undefined, especially when parenteral nutrition is used (Dissanaike et al. 2007; Gramlich et al. 2004; The Veterans Affairs Total Parenteral Nutrition Cooperative Study Group, 1991). Hence, both over- and underfeeding will be prevented when the caloric intake matches the actual EE (Singer et al. 2010). However, some recent data (Arabi et al. 2011; Casaer et al. 2011; Rice et al. 2012; Vincent and Preiser, 2013) challenge the concept of EE as a guide for the prescription of calories, when a non-inhibitable endogenous production of glucose provides a large amount of calories during the early phase of critical illness. Other recent studies (Heidegger et al. 2013; Singer et al. 2011) found some clinical benefit of an IC-guided caloric intake, as compared to an exclusive enteral regimen, irrespective of the EE. In any case the accurate measurement of EE can merely help to prevent overfeeding in long-staying patients.

The Total EE (TEE) includes three components (see Figure 1): the Basal Energy Expenditure (BEE) or Basal Metabolic Rate (BMR), the energy used during substrate metabolism, including the diet-induced thermogenesis (DIT) and the energy required for physical activity (Haugen et al. 2007; Lev et al. 2010). The BEE is the energy required to maintain the body's basic cellular metabolic activity and organ functions (Haugen et al. 2007). BEE is very close to the resting energy expenditure (REE) when a postabsorptive individual is resting, but not in critically ill patients (Lev et al. 2010).

EE is extremely difficult to predict during critical illness. Traditionally, the EE of a critically ill patient is considered to be higher than the EE predicted for a matched healthy subject, although some ICU patients could be hypometabolic (Magnuson et al. 2011; McClave et al. 2013; Siirala et al. 2010). The prediction of EE is further complicated by its large variations over a stay in ICU (Uehara et al. 1999). Even the complex predictive equations based on different anthropometrical and vital parameters with or without correction stress factor (Frankenfield et al. 2009; Frankenfield et al. 2012; Frankenfield, 2011) are inaccurate in critically ill patients (Avitzur et al. 2003; Frankenfield et al. 2009).

A calorimeter is designed to measure EE, calculated from the amount of exhaled of carbon dioxide (VCO2) and consumed oxygen (VO2) (Haugen et al. 2007).

Principles of Calorimetry (Table 1)

Calorimetry is a measure of the caloric expenditure of a patient through the production of heat by metabolic process (Haugen et al. 2007). As direct calorimetry cannot be used at the bedside, indirect calorimetry (IC) was elaborated by measuring respiratory gases (Haugen et al. 2007). The VO_2 and VCO_2 are measured by analysis of the gas exchanged, and the modified Weir equation allows the calculation of TEE (see Table 1, equation 1) (Weir, 1949). The measurement of VO_2 and VCO_2 is calculated as the difference in the volume of inspired and expired air multiplied by the concentration of the content of O_2 and CO_2 respectively (see Table 1, equation 3). Because the small difference between inspiratory (Vi) and expiratory volumes (Ve) is difficult to measure, Vi is commonly calculated using the Haldane transformation, which assumes that inert gas nitrogen (N2) is constant in both inspired and expired gases (see Table 1, equation 4). In this simplification the risk of error on the denominator increases as FiO_2 increases, espe-

Figure 1. Components of the Energy Expenditure

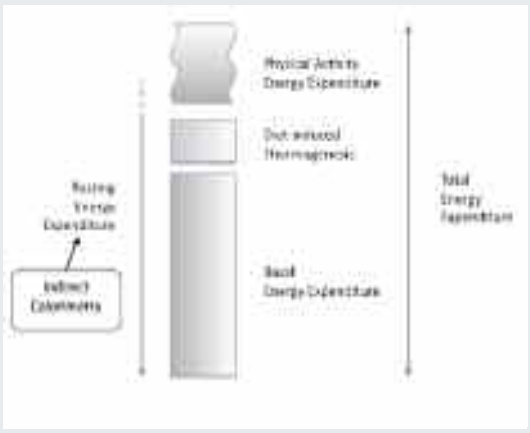

Table 1. Equations Used in Indirect Calorimetry

Equation 1 (Haugen et al. 2007)
Energy Expenditure (kcal/d) = [(VO_2 x 3.941) + (VCO_2 x 1.11) + (uN_2 (g) x 2.17)] x 1440
Equation 2 (Bursztein et al. 1989; Haugen et al. 2007)
Energy Expenditure (kcal/d) = [(VO_2 x 3.941) + (VCO_2 x 1.11) x 1440
Equations 3 (da Rocha et al. 2006; Haugen et al. 2007)
VO_2 (L/min) = Vi(FiO_2) – Ve(FeO_2)
VCO_2 (L/min) = Ve($FeCO_2$) – Vi($FiCO_2$)
Equations 4 (da Rocha et al. 2006; Haugen et al. 2007; Walsh, 2003)
If Vi = [FeN_2 / FiN_2] Ve then FeN2 = (1 - FeO_2 - $FeCO_2$) and FiN2 = (1 - FiO_2 - $FiCO_2$); and if $FiCO_2$ is neglected:
VO_2 = [(1 - FeO_2 – $FeCO_2$) x (FiO_2 – FeO_2)Ve] / (1-FiO_2)
Equation 5 (Bursztein et al. 1989)
REE = VO_2 x 4.838 x 1.44
Equations 6 (Bursztein et al. 1989; Lev et al. 2010)
EE (kcal/d) = 3.91 (VO_2) (L/d) + 1.1(VCO_2) (L/d) – 3.34 (uN) (g/d)
Carbohydrate use = 4,45 VCO_2 – 3,21 VO_2 – 2,87 uN_2
Fat use = 1,67 VO_2 – 1,67 VCO_2 – 1,92 uN_2
VO_2 : Consumption of O_2; VCO_2 : production of CO_2; Vi : Inspiratory Volume; Ve : Expiratory Volume; uN_2 : urinary nitrogen component; FiO_2 : fraction of inspired oxygen; FeO2 : fraction of expired oxygen;

cially when FiO_2 is above 60% or when anaesthetic gases or nitric oxide are inhaled (Walsh, 2003). REE can be derived from VO_2 alone (see Table 1, equation 5) if the patient does not have respiratory failure and is in a stable condition. In conditions of acute lung injury this equation does not take into account the VO_2 of the lung, which may reach 15-20% of the total VO_2 (Bursztein et al. 1989). The urinary nitrogen content (uN_2) is often neglected because it only accounts for less than 4% of the TEE (see Table 1, equation 2) (Bursztein et al. 1989; Haugen et al. 2007). The Respiratory Quotient (RQ) is the ratio between VCO_2 and VO_2 (VCO_2/VO_2), and represents the relative metabolism of the different macronutrients. The carbohydrate and fat oxidation could be calculated from these measures (see Table 1, equations 6) (Bursztein et al. 1989). A value of 1.0 corresponds to a complete glucose oxidation. RQ of the proteins is less and lower for the lipid. The physiologic human range is 0.67-1.2. If the value is outside a range of 0.7 to 1.0, the quality of the measurement should be questioned (Compher et al. 2006; Haugen et al. 2007).

IC was validated compared to reference techniques (direct calorimetry, double labelled water technique) (Lev et al. 2010). IC was largely used in various categories of ICU patients (Kemper et al. 1992; Kyle et al. 2012). The ICU nutrition guidelines proposed the use of IC instead of predictive equations when it is available, particularly for lean and obese patients, and in patients with burn injuries and liver diseases (Kreymann et al. 2006; McClave et al. 2009; Singer et al. 2009). The integration of the IC in a computerised information system allows automatic calculation of the caloric debt (Dvir et al. 2006; Berger et al. 2006). The respiratory quotient (RQ) could also be used to assess the presence of under- (RQ < 0.85) or overfeeding (RQ > 1.0), but with a low sensitivity and specificity (McClave et al. 2003a). RQ >= 1.0 may be associated with reduced tolerance and mild respiratory compromise (McClave et al. 2003a).

The devices are described as closed-circuit indirect calorimeters if the inspired air comes from an air or oxygen tank inside the calorimeter. However, open-circuit indirect calorimeters (inspired air source is room air or ventilator) are the most widely used in ICU (Lev et al. 2010). The expensive, cumbersome and oldest machines were composed of a Douglas bag in which the expiratory gases were blended (Schoeller 2007). The commercial metabolic cart contains a mixing chamber inside and gas analysers. The expired gas is mixed with a flow of room air, large enough to ensure constant total flow. The Deltatrac II (Datex-Ohmeda, General Electrics, Finland) was the most frequently used and classical IC, but is no longer marketed (Schoeller 2007). Technical expertise and regular calibration were needed, such as warming delay (about 20-30 minutes) (Lev et al. 2010). Only a few dedicated centres still use these devices.

How Should We Use an Indirect Calorimeter? (Figure 2 and Table 2)

In a systematic review, Compher et al. define best practice methods to measure the REE in adults. A minimum rest of 10 to 20 minutes, and a room temperature of 20 to 25°C are requested (Compher et al. 2006). Measurements recorded during the first five minutes are discarded. A five minute period with <= 10% coefficient of variation for VO_2 and VCO_2 would be suitable (Compher et al. 2006; Lev et al. 2010). If steady state is not achieved, two or three non-consecutive measures improve accuracy. Smyrnios et al. compared measurements of 24-hour duration with a 30-minute duration and found no major differences (Smyrnios et al. 1997). The best time was found to be around noon. For unstable patients, a two-hour measurement was

Figure 2. Patient with an Indirect Calorimeter

demonstrated to minimise the rate of error (Smyrnios et al. 1997; Zijlstra et al. 2007). McClave et al. showed that taking the mean REE from a 5-minute steady state (10% variation) provides the most accurate value, which can be extrapolated to represent the 24-hour total REE (McClave et al. 2003b). In a population of critically ill children, a reduction of the interval of steady state resulted in a significantly greater number of patients reaching steady state without significantly changing accuracy (Smallwood and Mehta 2012). For a patient not ventilated, a canopy system could be used but required a high gas flow to avoid carbon dioxide accumulation and the need to detect very small differences in gas concentration (Walsh 2003).

Any air leak in the circuit (endotracheal tube cuff leak, leaking chest tubes or bronchopleural fistulas) (Compher et al. 2006; Lev et al. 2010) will affect the measure as will any procedure that affects gas exchange (extracorporeal CO_2 removal or extracorporeal membrane oxygenator or renal replacement therapy) (Lev et al. 2010).

> *"Energy Expenditure is extremely difficult to predict during critical illness"*

Connecting the indirect calorimeter to ventilators with large bias flow (flow-triggering) could be a problem (Lev et al. 2010).

An increase of the energy consumption occurs also when the patient was agitated, suffered from pain or had fever or shivering (Chiolero et al. 1997) Lastly, attention must be paid to the presence of secretions or condensation retained in the tubing of the ventilatory circuit (McClave et al. 2013). A high or low RQ could also be calculated if the proportion of fat and glucose is too high or too low (Haugen et al. 2007). Finally, the device must be adequately and regularly calibrated (Compher et al. 2006; Haugen et al. 2007).

Performance of Currently Available Indirect Calorimeters: Pitfalls and Limitations

Some handheld indirect calorimeters have been developed by the industry with breath-to-breath analysis (Haugen et al. 2007). These devices collect expired air via a face mask or canopy or directly from the exit port of the ventilator (Lev et al. 2010). The performance of the MedGem (HealtheTech, Golden, CO), a handheld device placed inside the canopy was validated against the reference Deltatrac (Datex-Ohmeda, Madison, WI) device in a healthy population (Stewart et al. 2005).

Recently, some devices were proposed for critically ill patients. M-COVX (metabolic monitor in S/5 Critical Care Monitor, Datex-Ohmeda) was compared to Deltatrac II in twenty mechanically ventilated, critically ill patients and was found to yield an acceptable intra-patient reproducibility (less than 2% for VO_2, VCO_2 and REE) (McLellan et al. 2002). In contrast, a comparison of the Deltatrac II to the same M-COVX and the Evita 4 monitoring devices in 43 ventilated critically ill patients found poor agreement despite good correlation between measurements (Singer et al. 2006). Deltatrac MBM 100 (Datex) was compared with Vmax Encore 29n (SensorMedics) in healthy subjects and a lack of accuracy, comparability and transferability of the results was shown, but could be improved by a post-calorimetric calibration (Schadewaldt et al. 2013). However, this time-consuming procedure was unrealistic in a common clinical setting. Similar disappointing results were found in healthy subjects with the Deltatrac II compared to five other devices: MedGraphics CPX Ultima, MedGem, Vmax Encore 29 System, TrueOne 2400, and Korr ReeVue (Cooper et al. 2009). Sundström et al. compared Deltatrac to more recent calorimeters in mechanically ventilated patients, the Quark RMR (Cosmed, Italy) and the CCM Express (MedGraphics Corp., St Paul,

Minneapolis, USA) and found conflicting estimations of EE (Sundstrom et al. 2013). Another comparative study found the same results (Graf et al. 2011). In these two last studies, the Quark RMR device showed better results than the CCM express but with unacceptable variations for the clinical purpose.

The devices are usually expensive (€25,000 to €40,000) and the manpower cost is high (Cooney and Frankenfield, 2012). The period of measurement is long and a warming time has to be awaited before starting the process. The calibration time and the cost of the tank of gas for calibration could also be barriers. Davis et al. calculated that omitting IC could save $33,000 in their surgical ICU, but in their study the predictive equation performed well in contrast to other studies (Avitzur et al. 2003; Cutts et al. 1997; Davis et al. 2006; Frankenfield et al. 2009). The limitations cited above of such ventilation with no more than 60 % FiO_2, no

Table 2. Rules For Performing Indirect Calorimetry

- Respect warm-up of the calorimeter recommended by the manufacturer;
- Calibrate the device according to the manufacturer recommendation (alcohol burning kit or gas tank furnished);
- Exclude every leak (chest tubes, bronchopleural fistulas...);
- Consider the mode of ventilation (leak, flow trigger);
- FiO_2 should be less than 60% (up to 70% with MCOVX) with no recent fluctuation;
- Positive end-expiratory pressure (PEEP) lower than 12 mmHg;
- No use of Nitric oxide or anaesthetic gas;
- No change in the ventilator setting 1 to 2 hours before the IC measurement;
- Haemodynamic and temperature stability;
- No renal replacement therapy, extracorporeal membrane exchange therapy;
- Secretion or excessive humidity in the circuit;
- No active physical activity or physiotherapy during the measurement;
- No respiratory distress, polypnea or respiratory instability; and
- No suctioning during the measurement.

References: (da Rocha et al. 2006; Lev et al. 2010)

high pressure (PEEP above 12 mmHg), no other gas inhaled or gas exchange therapy are also major drawbacks limiting the number of patients that could benefit from the technique.

A recent validation of IC (Siirala et al. 2012) in healthy volunteers undergoing pressure controlled non-invasive ventilation support was published, but numerous flaws exist and other confirmatory studies are needed (Esquinas and Koksal 2013).

The IC measures the REE that is extrapolated to the rest of the day but physical activity is not included. In clinical practice the experts recommend to add 10 to 15% to the RMR measured to approach the TEE (Schoeller, 2007). However, this activity factor is difficult to estimate in ICU. Physiotherapy, the patient's agitation and the early mobilisation that is recommended nowadays are difficult to evaluate. Even if a continuous recording is made, the pitfalls secondary to a higher respiratory rate (Walsh, 2003) and respiratory instability precludes a precise evaluation of the TEE.

What's Next?

Definitely more appropriate devices are needed to assess the clinical relevance of using an indirect calorimetry-guided approach for the management of caloric prescription in critically ill patients. A task force of experts has been launched by the European Society of Clinical Nutrition and Metabolism (ESPEN) to cooperate with industrial partners on the development of reliable indirect calorimeters useable in ICUs. In parallel the TICACOS study (NCT01479673) aims to assess the necessity for measuring daily resting energy expenditure as a guide for nutritional support (Singer et al. in progress). The research hypothesis of this study is that tight caloric control will reduce the rate of new infections. ■

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DELAYED ICU ADMISSION AND ITS IMPACT ON MORTALITY

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Delayed admission of a patient in ICU is associated with a potential increase in mortality. This delay can be due to several factors, such as recognition of severity criteria, triage strategy and paucity of available ICU beds. The identification of these factors is important to identify targets for improvement of ICU patient early management.

A paucity of ICU beds is a major concern for many countries. A shorter time from critical illness onset to ICU admission is associated with better patient outcomes and lower rates of complications related to the ICU stay and critical illness, in both the patient and the relatives. Thus to shorten the time to admission, the number of ICU beds must be appropriate for the population served. However, advances in modern medicine, especially for the most vulnerable patients (cancer, leukemia), associated with the ageing of the population, leads inexorably to an increase in the number of patients admitted to intensive care. In this context, triage plays a pivotal role in optimising ICU admission, taking into account recognition of severity criteria, proposal of the patient to the consultant intensivist, and final acceptance, refusal or reassessment of the patient for ICU admission. It is important to integrate the triage strategy and the potential risk of delayed admission to optimise ICU admission, especially when resources in ICU beds are limited.

Recognising the Severity of Symptoms in the Emergency Department

Delay in recognising the gravity of signs motivating transfer to intensive care has been the theme of an extensive literature for nearly 15 years, which always leads to the same conclusion: delayed implementation of specific care for patients requiring resuscitation due to a failure to recognise severe symptoms is a source of mortality. Rivers et al. (Rivers, Nguyen et al. 2001) were the first to show that aggressive and early management of patients with septic shock could reduce mortality at day 28. However, such specific treatment could be carried out in the emergency department, and does not necessarily imply an immediate transfer to ICU. O'Callaghan et al. observed that patients transferred to ICU with delay needed more invasive mechanical ventilation support (O'Callaghan et al. 2012).In the context of community-acquired pneumonia where specific care (mechanical ventilation, noninvasive ventilation, physiotherapy) is probably the most urgent, Restrepo et al. (Restrepo, Mortensen et al. 2010) found that patients transferred secondarily after primary transfer to a conventional ward had a mortality significantly higher than those transferred sooner (23% vs. 47% ; $p = 0.02$), while they had the same clinical, biological and radiological emergency admission specifications. In a retrospective study of more than 50,000 patients, Chalfin et al. (Chalfin, Trzeciak et al. 2007) observed that critically ill patients who had more than a six hour delay in ICU transfer had an increased ICU mortality (17.4% vs. 12.9% ($p<0.001$).

To enable support without delay to these specific categories of patient, and avoiding misdirection and transfer from the conventional sector several areas for improvement do exist. Firstly, recognition of severity of signs by nurses can be improved by nurse education. Experienced nurses with several years of activity are faster to recognise patients requiring organ support (Cioffi 2000). As for doctors, nurses require training to recognise adequately severity of patients (McGloin et al. 1999). Secondly, development and validation of several severity scores (Early Warning Score (Morgan et al. 1997); VitalPAC EWS (Prytherch et al. 2010); Cardiac Arrest Risk Triage (CART) validated certificates (Churpek 2013)) led to the modelling and prediction of the risk of worsening and early detection of patients requiring specialised care and reducing delays to immediate care in the ICU. Finally, the implementation of rapid response teams aimed at the management of life-threatening emergencies outside the ICU to allow shorter periods of ICU admission has been proposed (Luca Cabrini 2012). However, their efficacy is controversial

(Devita et al. 2006; Luca Cabrini 2012). We can relate to this rapid response team idea by creating specific trainee graduates in the emergency field, particularly in Europe, for care and quick orientation of these patients. Sophisticated prehospitalisation emergency medicine may help to reduce the delay from the onset of critical disease to ICU admission (Nirula et al. 2010).

Criteria for ICU Admission and Refusal

Recommendations for ICU admission criteria have been published by societies of critical care (SCCM, ESICM), and can help the clinician in choosing whether to admit a patient to intensive care or not. The aim of such recommendations is both to admit patients requiring specific intensive care management, and to avoid the admission of patients too sick or too well to benefit from intensive care. However, Azoulay et al. demonstrated that these recommendations were only rarely applied (Azoulay et al. 2001). Several studies pointed out the fact that intensivists tend to admit patients in ICU even though they recognise that they should not (Vincent 1990; McNarry and Goldhill 2004; Giannini and Consonni 2006). A recent score, the "European Intensive Care Admission Triage Score", was developed by Sprung et al. to prevent the admission of those patients who do not benefit from their stay in the ICU and consume limited resources (Sprung et al. 2012). However, in this latter study, the admission strategy of patients to intensive care guided by a score did not result primarily in a restriction of indications but rather in an increase in the number of admissions despite a limited resource and with no benefit for these patients yet being demonstrated.

ICU Bed Availability

Refusal for ICU admission can be related mainly to three situations: 1) the patient is considered too sick to benefit; 2) the patient is considered too well to benefit, and 3) there is no bed available. This latter situation is a daily problem for intensivists (Singer et al. 1983). The proportion of patient refusal due to absence of beds available varies between 5% (Garrouste-Orgeas et al. 2005) and 20% (Robert et al. 2012). When a patient is proposed for ICU admission and there is no bed available, there are three different possibilities: emergency bumping of a patient to release a bed; transferring the patient to another ICU; or admitting the patient to a less specialised unit with the aim of reassessing the situation and proposing secondary ICU admission if it is still indicated. Whatever the chosen solution it leads to an additional delay in ICU admission or a risk of delivering an inappropriate level of care. Transfer to another ICU where a bed is available immediately is possible in countries where the different services are not geographically too far apart and / or transportation is provided by a specialist trained in the care of these patients, but not in large countries or where paramedics are responsible for transport (Wiegersma, et al. 2011). Nevertheless, even in the case of a transfer quickly assured by appropriate staff, Durairaj et al. found that these patients had worsening of their mortality (Durairaj et al. 2003). Robert et al. observed that patients refused for lack of available beds have a higher mortality compared with patients admitted to intensive care immediately (Robert et al. 2012). Meanwhile the lack of available beds influences the decision to admit or not resuscitate, since when there is no bed available doctors accept a smaller number of patients, patients who are younger and more severe (Iapichino, Corbella et al. 2010).

> *"Delayed implementation of specific care for patients requiring resuscitation due to a failure to recognise severe symptoms is a source of mortality"*

To fight against this delay to ICU admission, there are several ways to improve:

1. Perform resuscitation outside the ICU. Unfortunately, the literature suggests that even if the prognosis is closely related to the diagnosis and appropriate treatment, there are other factors that should be taken into account as part of unit-specific resuscitation (e.g. nurse / bed ratio, quality monitoring, presence of a practitioner 24/24h (Simchen et al. 2007)).
2. Reduce the ICU length stay in favour of strategies associated with reduction of mechanical ventilation such as sedation protocols (Kress et al. 2000).
3. Favour the development of intermediate care allowing a privileged circuit for rapid discharge of patients no longer under intensive care but needing more complicated care than on a regular ward.
4. It is important to anticipate periods of shortage, which may be related to a structural deficit or exceptional circumstances (e.g. terrorist attack, natural disaster) to reach the various categories of stakeholders in ICUs (Biddinger et al. 2013).

Meanwhile, it should be noted that the number of ICU beds related to population ratio is quite heterogeneous (Rhodes et al. 2012). Some statistical projections appear very far from the actual demand (Lyons et al. 2000; Carroll and Herbert 2004).

Conclusion

Delayed ICU admission aggravates the prognosis of patients awaiting transfer. Transfer to ICU is thus part of emergency treatment as well as antibiotic therapy in septic shock or coronary revascularisation in myocardial infarction.

In the context of limited resources, it is important to develop tools to provide adequate care to those most able to take advantage of it in order to ensure constant availability of beds and resuscitation teams thanks to the training of various stakeholders, efficient triage policies and to promote intermediate care units.

It would be of interest to determine with homogeneous criteria the appropriate number of ICU beds for a population served. The ICU bed / population ratio is a key issue in the health policy of a country. ■

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AUTHOR GUIDELINES

ICU MANAGEMENT

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Thank you,
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SEPSIS IN CRITICAL CARE

AN INTERVIEW WITH **PROFESSOR DJILLALI ANNANE**

Professor Djillali Annane is Professor of Medicine and Dean of the Medical School at the University of Versailles, Paris. He is the director of the general intensive care unit at Raymond Poincaré, Assistance Publique Hôpitaux de Paris (APHP). The unit is the largest ICU at the University Hospital of Paris, and has 36 beds, half of them high intensity beds, and half step-down units. Prof. Annane is also Director of the Laboratory Neuroendocrine Response to Sepsis, University of Versailles and Director of the Centre for Clinical Research and Technological Innovation, INSERM, Paris.

Your team recently reported on the recombinant human activated protein C for adults with septic shock. Why was the trial suspended?

Our main research area is sepsis: understanding the mechanism and investigating treatments. In 2007 we started a national multicentre randomised trial that was fully independent from the pharmaceutical industry, to evaluate the benefit-to-risk ratio of activated protein C in patients with septic shock. This was a double-blind randomised trial that was funded by the French Ministry of Health. We used commercialised activated protein C, which the pharmacists at the hospital masked for the purpose of the trial. In October 2011 when Eli Lilly and Company decided to withdraw Xigris ® from the market and the drug was no longer available, Lilly declined to provide us with the treatment and its placebo. Hence, there was no way to continue the trial, and it was terminated after 411 patients were included.

What were the findings before that point?

First, we have investigated a population with severe septic shock. The observed mortality at 90 days in placebo-treated patients was about 45%, which is almost twice as high as the mortality observed in the PROWESS-SHOCK trial. We enrolled septic shock patients in whom physicians would be happy to have an adjuvant therapy to improve the chance of survival.

The second important finding is the lack of evidence of any benefit on survival or on any other outcome from activated protein C. Taking this finding together with the findings from the PROWESS-SHOCK, ADDRESS, and RESOLVE trials, one may conclude that activated protein C failed to prove any benefit in children and adults with sepsis, regardless of disease severity.

Does this resolve the question, or are there still unanswered questions?

As far as activated protein C for sepsis is concerned, I do not believe there are still unanswered issues. Definitely the drug was investigated in children and adults, and in adults it was investigated in a broad range of disease severity, and, in these different cases with different baseline risk of death, activated protein C repeatedly did not show any benefit on any outcome, including survival, need and duration of vasopressor therapy, mechanical ventilation or renal replacement therapy, or length of stay in the ICU or at hospital.

Recently a number of big fluid trials have been conducted. Where do we stand today with fluid resuscitation in critically ill patients and what future studies are required in this area?

First, I think the important take home message is that fluid therapy is by far the commonest treatment in the intensive care unit, and there are thousands of patients being treated daily with one or more types of fluid. Basically there are two families of fluid - crystalloids and colloids. Crystalloids offer the theoretical advantages of being cheaper, less allergic, and less toxic than colloids. Colloids have the theoretical advantage of faster recovery, of haemodynamic stability. What did we learn from Crystalloid Versus Hydroxyethyl Starch Trials (CHEST) and Hydroxyethyl Starch 130/0.42 versus Ringer's Acetate in Severe Sepsis (6S) trials? First, and this is important to interpret these data, these trials compared one molecule with another – CHEST compared Voluven® to normal saline, and 6S compared Tetraspan 6%® to Ringer acetate (Sterofundin ISO®). It is important to bear in mind that these trials did not compare all crystalloids with all colloids. Hence, they can only answer that there was no evidence that most recent starch solutions are superior to normal saline or Ringer's Acetate. These findings do not mean that there are no differences between the two families of fluids, crystalloids and colloids. However, consistent findings within these trials included an increased risk of renal injury with starches. Thus, in practice one should refrain from using these starch solutions as a first line treatment, and one should prefer normal saline or Ringer's Acetate. This is basically the recommendation in the update of the Surviving Sepsis Campaign guidelines.

In this respect, can you please give us a short overview of the most significant findings of the CRYSTAL study?*

I would like to highlight that these findings are as yet unpublished. We presented the main findings at the 2013 ISICEM meeting in Brussels. This pragmatic trial compared a strategy based on crystalloids only to a strategy based on colloids only for the whole ICU stay. This multinational study was conducted in France, Belgium, North Africa and Canada, and included close to 3,000 patients. The trial was designed to show the superiority of crystalloids over colloids based on a systematic review of the information available at this time. Unexpectedly, at 90 days, a strategy based on crystalloids was associated with

more deaths than a strategy based on colloids. These data have not yet been published in a peer-reviewed journal, and should be taken with caution until publication.

Do RCTs such as these provide clear evidence for the intensivist? Are they still the gold standard?

I think that RCTs are of course still the gold standard. Nevertheless, in the very near future an increased interest in data derived from big ICU databases, regulatory agencies such as FDA and the European Medicines Agency (EMEA), the NHS, the Ministry of Health in France, and many other public or private institutions, are giving more and more attention to and credit to big databases, as a potential new tool for investigating treatment effects.

This interview will form part of our edition on Organ Donation. What do you think poses the biggest challenge for the intensivist when it comes to organ donation?

Organ donation is really important, given that organs are still missing for transplant recipients. Many people are still dying while waiting for an organ to be available. The ICU is a location where people die, where brain dead patients are admitted, and therefore is a location where potential organ donors could be found. However, the management of organ donors cannot be done in all ICUs. I think that the management of these patients should be limited to a few ICUs with trained staff. In different regions of a country, there should be one or two ICUs that are responsible for dealing with organ donors. Indeed, undoubtedly the way these patients are managed is very important for the quality of organs to be transplanted and subsequently a key factor for successful transplantation. In addition, this organisation in a country may also shorten the time from identification of an organ donor and the time an organ is transplanted to a recipient. It may help improve the efficiency of organ donation.

What do you see as 'hot topics' in intensive care medicine currently?

Firstly, we are entering a new era in the way we are doing clinical research in the ICU. In the past few years we already have shifted from moderately sized RCTs to large RCTs, and this will continue in the future. Networks that have been developed in several countries are increasingly interacting together in such a way that in a couple of years most ICU trials will be conducted through internationally linked, national networks. This will definitely present a big jump in clinical research in the ICU, allowing fast conduct of large, mostly academic-driven RCTs.

The second hot topic is the emergence in ICU practice of molecular biology. That will progressively shift patients' management from ICU based treatments to personalised ICU patient-based treatments. This will be true for sepsis, ARDS, trauma, haemorrhage and for a number of critical illnesses.

What research are you working on now?

We are continuing trying to understand the mechanisms of sepsis and to develop treatments for sepsis. Currently we are working on the modulation of the adrenergic system as a therapeutic approach to sepsis. Briefly, we think that while septic patients require alpha agonists like norepinephrine for a haemodynamic purpose, and may require beta 2-agonists for metabolic purpose, they also may require beta 1-antagonists for immune purpose. We are looking at ways to fine tune the adrenergic system during sepsis. We are doing a set of experiments in small and large animals, and, in 2013, we may start a phase II trial in patients with sepsis in collaboration with 5 to 6 ICUs across France. If these phase II trials are up to expectation, we will move to a phase III trial in 2014.

> *"As far as activated protein C for sepsis is concerned, I do not believe there are still unanswered issues"*

What do you see as the most significant breakthroughs in intensive care medicine recently?

That's a tough question! If one looks at recent published RCTs done in the ICU one will see that most of them resulted in negative trials, and sometimes even the experimental treatment harmed patients. For example, the 6S trial found higher mortality rates with a starch solution in patients with septic shock.

A very recent trial showed a dramatic improvement in survival in ARDS patients by using the prone position. I think that this is likely one of the most important advances that will change practices.

Intensive care is a young specialty. Intensivists and trialists in intensive care are still learning how to do clinical trials. I believe we will see more positive trials, while getting better knowledge both in the understanding of diseases and in the methodology of clinical trials. We will include molecular tools to select the patients and to monitor treatments. We will have more skilled investigator sites relying on strong, internationally linked clinical networks. ■

* University of Versailles. Efficacy and safety of colloids versus crystalloids for fluid resuscitation in critically ill patients. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2013 June 8]. Available from: http://clinicaltrials.gov/ct2/show/NCT00318942

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CRITICAL CARE IN SOUTH AFRICA

Critical care in South Africa is more developed than in other parts of Africa, but faces specific challenges, especially from infectious diseases. South Africa has the highest number of people infected with HIV in the world. TB is a particular health burden, and trauma from motor accidents and interpersonal violence is also prevalent. Social support is lacking and the country also has chronic health issues such as nutrition.

Private healthcare provides an integral part of the health services at all levels including ICU. Twenty percent of the population has medical insurance, which entitles them to care in private hospitals. Private hospitals account for sixty percent of healthcare spending and employ seventy percent of medical specialists. (Hodgson and Hardcastle 2013). The public healthcare system accounts for forty percent of spending (3.7% of GDP) and thirty percent of medical specialists (Hodgson and Hardcastle 2013). Most South Africans depend on an overstrained public service (Gopalan, D 2013, pers. comm., 30 June).

In the late 1960s there were some single function units such as post-operative ventilation of cardio-thoracic cases. The first multidisciplinary unit was opened in1970. Dr Neil Goodwin, the first full time intensivist on the African continent, was brought out from Sweden to run the unit with the assistance of dedicated anaesthetic registrars. In the mid 1970s units opened all over the republic, with the first Non-White ICU opening at King Edward VIII hospital in Durban in November 1974.

The Critical Care Society of Southern Africa (CCSSA) was formally constituted in 1978 following correspondence in the South African Medical Journal. The society is for all healthcare professionals involved in Critical Care – doctors, nurses, technicians, etc. The society is instrumental in guiding the development of Critical Care in South Africa, and plays an active role in setting of standards, training, negotiations with government and private health funders. The CCSA runs an annual national conference. (Gopalan, pers. comm.)

Most doctors working in ICU are not accredited. There are about 80 intensivists in South Africa. Critical Care has been recognised as a specialty in South Africa for more than ten years, and requires two years' training after first specialising in one of the disciplines such as Anaesthesiology, Internal Medicine, Surgery, and Paediatrics (Gopalan, D 2013, pers. comm., 30 June). The Sub-Specialty Certificate in Critical Care of the College of Physicians of South Africa is recognised by the Colleges of Medicine of South Africa –and comprises a written and oral examination.

Provinces are responsible for health. Currently only three provinces approach the international recommendation of ICU beds per 100,000. (Hodgson and Hardcastle 2013). Five out of nine provinces have fewer than 1: 100,000 beds. (Hodgson and Hardcastle 2013). Most ICUs in the private sector function as open ICUs as opposed to the state sector where ICUs are closed (Gopalan, D 2013, pers. comm., 30 June). Telemedicine has a very limited role, but would be useful where care is often remote. (Gopalan, D 2013, pers. comm., 30 June).

The challenges for critical care in the country are the health burden of infectious diseases and lack of infrastructure and resources – ICU beds, personnel, equipment and drugs. Inadequate transport, portering and laboratories also make functioning extremely difficult. Distances between referral centres and the lack of appropriate transfer facilities also impede care. (Gopalan, D 2013, pers. comm., 30 June). ■

Statistics

Total population	50,133,000
Gross national income per capita (PPP international $)	10,710
Life expectancy at birth m/f (years)	57/60
Probability of dying under five (per 1,000 live births)	47
Probability of dying between 15 and 60 years m/f (per 1,000 population)	474/407
Total expenditure on health per capita (Intl $, 2011)	942
Total expenditure on health as % of GDP (2011)	8.5
Physicians per 10,000 population	7.6
Population % over 60 (2010	7
Population % under 15 (2010)	30

Figures are for 2009 unless indicated. Source: World Health Organization Global Health Observatory http://apps.who.int/gho/data/view.main

Annual AIDS deaths	270,000
People living with HIV	5.6 million

Source: UNAIDS http://www.unaids.org/en/regionscountries/countries/southafrica/

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CRITICAL CARE 2013, DURBAN, SOUTH AFRICA, 28 AUGUST-1 SEPTEMBER

Dr. Dean Gopalan

The 11th World Federation of Societies of Intensive and Critical Care Medicine Congress will be held in South Africa for the first time later this year. ICU Management spoke to co-Chairs Dr. Dean Gopalan and Prof. Satish Bhagwanjee about what to expect.

What's new for Critical Care 2013?

We hope to make it a truly 'world' conference encompassing issues and challenges from all corners of the globe. It is the first time a conference of this nature and magnitude will be held on the African continent.

Our theme is "Critical Care for all … providing more for less." We hope to highlight strategies on rational utilisation of ICU resources to ensure maximal benefit. In addition, we hope to adopt and publicise a Durban Declaration, which we hope will make 10 key statements on critical care issues pertinent to the entire world.

What are the sessions delegates should not miss?

We have a wide range of sessions in different formats. There are plenaries, parallel sessions, workshops, debates, expert forums, industry symposia and round table discussions. All the main subjects will be covered. There will be particular emphases on sepsis, infectious diseases, ethics, resuscitation, ventilation and monitoring.

There will be sessions for paediatric, adult and nursing delegates. There will also be a large trade exhibition with the latest advances from the industry.

What controversial issues is the congress addressing?

There will be an attempt to highlight particular challenges faced by practitioners in extremely resource-constrained situations. Hopefully this will allow developed and underdeveloped regions to share strategies in a drive to going back to basics.

In addition, the current fluid management controversy will be tackled. Most of the big names from all the major recent publications will be in Durban.

There will also be sessions on ethics that will tackle many of the controversial issues including the management of HIV+ patients.

What do you see as the hottest topics in critical care currently?

Sepsis and infection control, ICU ethics, rationalisation of ICU resources, research in ICU and fluid management in ICU, especially surrounding colloid solutions.

Are there lessons developed countries can learn from developing countries when it comes to critical care?

Absolutely. One of the reasons we went with the theme "More for less" was to look at optimising the way critical care resources were being used in a country where resources are lacking and patients need to be managed in suboptimal conditions e.g. ward ventilation, inotrope use in wards. There are also ethical dilemmas regarding who gets turned away from ICU. Developing countries can also share their experience with managing infectious diseases e.g. HIV.

What does Critical Care 2013 offer to the upcoming intensive care specialist?

It offers them the chance to be exposed to high quality talks on a variety of subjects by the world leaders in the respective fields. It also gives them the opportunity to present whatever research they have in the form of posters/abstracts. There will be an opportunity for them to interact and network with similar colleagues from all over the world.

> *"It is the first time a conference of this nature and magnitude will be held on the African continent"*

What cultural and social activities are on offer for delegates to Durban?

Durban and South Africa in general are really noted for their hospitality. There will be an opening ceremony and welcome cocktail reception. There will also be an "African Carnival" beach party for all delegates on Saturday 31 August.

Delegates will have the opportunity to take city and regional tours to a variety of cultural sites. A full list of this is on the website. ■

For more information about the Congress visit **http://www.criticalcare2013.com**

AGENDA

AUGUST

28 – 1 11th World Federation of Societies of Intensive and Critical Care Medicine Congress
Durban, South Africa
www.criticalcare2013.com

28 – 1 ESPEN
Leipzig, Germany
www.espen.org

SEPTEMBER

8-11 ESOT (European Society for Organ Transplantation)
Vienna, Austria
www.esot.org

OCTOBER

5-9 25th ESICM LIVES 2013 Annual Congress
Paris, France
www.esicim.org

NOVEMBER

19-21 11th Doppler-Echocardiography in Intensive Care Medicine
Brussels, Belgium
www.intensive.org

29-30 3rd International Fluid Academy Day
Antwerp, Belgium
www.fluid-academy.org

DECEMBER

3 – 5 19th Postgraduate Refresher Course
Brussels, Belgium
www.intensive.org

8 – 11 Update on Renal Replacement Therapy
Rome, Italy
www.intensive.org

In our Next Issue

COVER STORY
The Kidney

SERIES: SEPSIS
Haemodynamic Resucitation in Sepsis

MANAGEMENT
Physical Restraint in the ICU

MATRIX
Abdominal Hypertension
Ventilation After Cardiac Arrest

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