ICU MANAGEMENT

THE OFFICIAL MANAGEMENT AND PRACTICE JOURNAL

VOLUME 12 - ISSUE 3 - AUTUMN 2012

gender

PLUS:

- Ventilator Associated Pneumonia: Breaking the Bridge
- Proper Use of Vasopressors in Septic Shock
- Does Intermediate Care Improve Patient Outcomes and Reduce Costs?
- Perioperative Nutrition in Upper Gastrointestinal Cancer Patients
- Interview with Andrew Rhodes. Developing and Harmonising a Prime Speciality

0 977137 775609 10

ORION PHARMA

INTRODUCING A NEW ERA IN ICU SEDATION:

Effective sedation. Effective response.

Depend on dexdor®:

- Maintain light-to-moderate sedation*
- Improve patient manageability*
- Facilitate better patient communication*
- Decrease time to extubation*

* Jakob S et al. JAMA 2012;307(11):1151–1160. Riker RR et al. JAMA 2009; 301(5):489–99.

dexdor®
[dexmedetomidine hcl] injection

Cooperative comfortable sedation

Indication: Sedation of adult ICU patients requiring sedation level not deeper than arousal in response to verbal stimulation (RASS 0 to -3). Dosage and administration: Hospital use only, by healthcare professionals skilled in management of patients requiring intensive care. Administer only as diluted intravenous infusion using controlled infusion device. Dose individualised to every patient and the infusion rate is given per hour. Switch patients already intubated and sedated to dexmedetomidine with initial infusion rate of 0.7 micrograms/kg/h and adjust stepwise within range 0.2 to 1.4 micrograms/kg/h to achieve desired sedation level. Consider lower starting infusion rate for frail patients. After dose adjustment, new steady state sedation level may not be reached for up to one hour. Do not exceed maximum dose of 1.4 micrograms/kg/h. Switch patients failing to achieve or adequate level of sedation with mainly increase to an alternative sedative agent. Loading dose not recommended. Administer propofol or midazolam if needed until clinical effects of *dexdor*® established. No experience in use of *dexdor*® for more than 14 days. Use for longer than this period should be regularly reassessed. *Elderly:* No dosage adjustment required. *Renal impairment:* No dosage adjustment required. *Hepatic impairment:* Caution advised, consider reduced dose. *Children aged 18 years:* Safety and efficacy not established. Contraindications: Hypersensitivity to dexmedetomidine or the excipients. Advanced heart block (grade 2 or 3) unless paced. Uncontrolled hypotension. Acute cerebrovascular conditions. Warnings and precautions: Intended for use in intensive care setting, use in other environments not recommended. Continuous cardiac monitoring required. Monitor respiration in non-intubated patients. Do not use as induction agent for intubation or to provide sedation during muscle relaxant use. *dexdor*® reduces heart rate and blood pressure but of higher concentrations causes peripheral vasoconstriction and hypertension. Not suitable in patients who will not tolerate lack of deep sedation and easy rousability. Users should be ready to use alternative sedative for acute control of agitation or during procedures, especially during the first few hours of treatment. Caution with: pre-existing bradycardia, high physical fitness and slow resting heart rate, pre-existing hypotension, hypovolaemia, chronic hypotension or reduced blood volume, severe ventricular dysfunction, the elderly, impaired peripheral autonomic activity (e.g. due to spinal cord injury), ischaemic heart disease or severe cerebrovascular disease, severe hepatic impairment, severe neurological disorders such as head injury and after neurosurgery. Reduce dose or discontinue if signs of hypotension or cerebral ischaemia. Additive effects may occur with other substances with sedative or cardiovascular actions. Some patients receiving *dexdor*® have been observed to be arousable and alert when stimulated; this alone should not be considered as evidence of lack of efficacy. Do not use as sole treatment in status epilepticus. Consider possibility of withdrawal reaction if patient develops agitation and hypertension shortly after stopping dexmedetomidine. Not recommended in malignant hyperthermia sensitive individuals. Discontinue treatment in event of sustained unexplained fever. Undesirable effects: Very common (≥1/10): Bradycardia, hypotension, hypertension. Common (≥1/100 to <1/10): Hyperglycaemia, hypoglycaemia, agitation, myocardial ischaemia or infarction, tachycardia, nausea, vomiting, dry mouth, withdrawal syndrome, hyperthermia. Uncommon (≥1/1,000 to <1/100): Metabolic acidosis, hypovolaemia/anuria, hallucination, atrioventricular block first degree, cardiac output decreased, dysphoria, abdominal discomfort, drug ineffective, thirst. See SPC for further details. Pack sizes: 5 x 2 ml ampoules, 25 x 2 ml ampoules, 5 x 4 ml vials, 4 x 10 ml vials. Marketing authorisation holder: Orion Corporation, Orionintie 1, FI-02200 Espoo, Finland. *dexdor*® is a registered trademark. Date of Preparing Information: Sep 2013.

www.dexdor.eu

GENDER

Jean-Louis Vincent

Editor-in-Chief
ICU Management

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

jlvincen@ulb.ac.be

Even in a world full of innovation, developments and advanced intensive care medicine, there are areas and issues within the realm of critical care that are overlooked, at least on a comprehensive scale. As more studies and research projects are completed, and new experiences and knowledge are shared across the speciality, the quality and standard of intensive care medicine and processes are improving in bounds on many levels. Still though, grey areas and hidden cracks are present in the framework, many of which are being explored by researchers and physicians in the hope of resolving some questions, raising awareness of existing disparities or gaps in care, and supporting positive change.

One area of intensive care medicine that warrants further recognition and research is that of the relationship between the sex and gender of a patient and the intensive care they receive. This is the topic of focus in this issue of ICU Management, with the first article from Jennifer Innis and Dr. Arlene Bierman, from the University of Toronto, Canada, suggesting application of a sex and gender lens to quality improvement, in order for care access, quality, and outcomes across genders to be optimised. Second in our Cover Story is a stimulating article entitled "Unraveling the Effect of Gender on ICU Mortality". Dr. Irit Nachtigall and her team express the importance of a more detailed understanding of differences in clinical presentation, course of diseases, and cure processes in patients of different gender, with much of the research they present centring on response to sepsis.

This focus on the sex and gender of a patient is subsequently brought across to our Nutrition series. Here, Dr. Sandra Stapel and her colleagues from VU University Medical Center in the Netherlands describe several gender differences that relate to optimal nutrition in intensive care, including their hypothetical implications for the patient. Another specially focused nutrition piece, "Perioperative Nutrition in Upper Gastrointestinal Cancer Patients", follows, in which Prof. Christophe Mariette provides current information and advice. Knowledge of the nutritional status of individual patients in this sub-group is expressed as essential not only in identifying malnourished and non-malnourished patients, but also in allowing treatment adaptations along each step of the multimodal oncological treatment path, with standard enteral nutrition (EN) and immunonutrition serving as a complementary therapeutic limb.

As we move into our Matrix section, we look at a topic explored in our Cover Story, sepsis, from a different angle. Here, Drs. Marc Leone, Benoit Ragonnet and Claude Martin portray in comprehensive detail the proper use of vasopressors in septic shock, putting across key learning points. Following this, another infection, this time ventilator associated pneumonia (VAP) is the focal point. Drs. Andrea Coppadoro, Riccardo Pinciroli, and Lorenzo Berra look at innovative strategies for preventing the infection by targeting the role of the endotracheal tube as the main pathogenic factor involved in its development. Drs. Mariam Alansari and Khalid Maghrabi from Riyadh, Saudi Arabia, write the final feature in this section, which focuses on imaging efficacy. They put forward that unnecessary chest x-rays need to be eliminated and replaced by an alternative technique. As well as suggesting guidelines for efficient routine and on-demand x-ray use, they also propose ways in which future studies on the subject can be best designed.

Prof. Andrew Rhodes is the subject of our interview, which focuses on his aspirations and recent achievements as President of the European Society of Intensive Care Medicine (ESICM). Then, in our management section, I question the role of intermediate care units in reducing costs and improving outcomes, and suggest rather that efficiency could be improved by combining intermediate care and intensive care in one unit.

To conclude, our Country Focus features two articles that examine the Portuguese healthcare sector. The first, written by Paulo Alexandre Boto and Fernando Leal da Costa, assistants to the Minister for Health, provides a comprehensive overview of healthcare in the country, including a proposed sustainability plan from the national Ministry of Health. Second is a feature from Drs. Luís Coelho and João Gouveia that concentrates on the intensive care sector. They discuss recent challenges in the Portuguese sector, some of which other countries are also enduring, such as those stemming from the economic crisis and an ageing population, and look at areas where new strategies are needed.

Please send your responses to me at **editorial@icu-management.org.**

Jean-Louis Vincent

Join us in 2013

33rd International Symposium on Intensive Care and Emergency Medicine

BRUSSELS MEETING CENTER (SQUARE)

MARCH 19-22, 2013

Hôpital Erasme | ULB

CME Accreditation

Plenary Sessions, Mini-Symposia,
Workshop, Technical Forums, Round Tables, Tutorials, Posters

Endorsed by:

European Society of Intensive Care Medicine
Society of Critical Care Medicine
American Thoracic Society
European Society for Emergency Medicine
European Shock Society
The Institute of Critical Care Medicine
The Canadian Critical Care Society
Australian and New Zealand Intensive Care Society
International Pan Arab Critical Care Medicine Society
World Federation of Societies of Intensive and Critical Care Medicine
International Sepsis Forum

Meeting Chairman: JL Vincent
Email: jlvincent@ulb.ac.be

Manager: V De Vlaeminck
Email: veronique.devlaeminck@ulb.ac.be

Dept of Intensive Care
Erasme University Hospital
Route de Lennik, 808,
B-1070 Brussels, Belgium

Phone 32.2.555.32.15/36.31,
Fax 32.2.555.45.55
Email: symposium@ulb.ac.be

Website: http://www.intensive.org

Deadline for abstract submission: December 15, 2012

ICU Management

is the Official Management and Practice Journal of the International Symposium on Intensive Care and Emergency Medicine and was previously published as Hospital Critical Care.

INDUSTRY NEWS

European STEMI Guidelines Emphasise Care Coordination

The European Society of Cardiology (ESC) guidelines for the management of patients with acute ST-elevation MI (STEMI) anticipate spurring efforts to improve the speed and efficiency of STEMI care in Europe.

The new recommendations, which were announced at the European Society of Cardiology 2012 Congress on 26 August, suggest a new standard for time from medical contact to ECG of 10 minutes. Two hours is the limit of acceptable delay for a patient transferred from a non-PCI (Percutaneous Coronary Intervention) centre to a PCI centre, though the target should be 90 minutes, suggest the guidelines. If PCI within two hours of presentation appears to be impossible, then fibrinolysis should be administered within 30 minutes, it is recommended.

The guidelines suggest that if fibrinolysis succeeds, angiography can begin with the expectation of PCI within three to 24 hours. If fibrinolysis fails, the interventionalist should consider PCI admission as quickly as possible.

Europe does not yet have a pan-European STEMI registry, but some countries have national registries, highlighted Dr. Gabriel Steg, chair of the task force that wrote the new recommendations.

The guidelines recommend implanting drug-eluting instead of bare-metal stents in patients who are not contraindicated for dual antiplatelet therapy and are likely to stick to their prescribed regimen. They also advise newer antiplatelet drugs, such as prasugrel or ticagrelor over clopidogrel.

The document also supports employing transradial catheterisation rather than the transfemoral approach, but only in the hands of experienced operators.

Many areas in need of further research are identified in the guidelines, ranging from questions about early prehospital care to long-term management.

The new document replaces the guidelines released in 2008 and complements the non-STEMI treatment guidelines released at last year's ESC congress.

www.medscape.com

Reference:

Steg G et al. (2012). ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). Eur Heart J; DOI:10.1093/eurheartj/ehs215. Available at: http://eurheartj.oxfordjournals.org/

RESEARCH NEWS

Elevated Glucose Levels Predict Mortality in Pneumonia Patients

Non-diabetic patients who have elevated serum glucose levels when they are admitted to the hospital presenting community-acquired pneumonia (CAP) have an increased risk of dying within 90 days compared with normoglycemic patients with the same illness, suggest studies presented at the European Respiratory Society (ERS) 2012 Annual Congress in Vienna, Austria, on 2 September.

High serum glucose levels predispose people to CAP by increasing the risk for aspiration, decreasing immunity, and causing impaired lung function, a Community Acquired Pneumonia Competence Network (CAPNETZ) study has found.

The study, headed by Dr. Philipp M. Lepper from the University Hospital of Saarland in Homburg, Germany, evaluated whether acute dysglycaemia could predict a poor outcome in patients with CAP who had not been diagnosed with diabetes.

"Increased serum glucose levels at admission is a risk factor for death among patients with community-acquired pneumonia. The risk for mortality starts to increase when serum glucose levels are slightly increased but remain below the defined threshold for overt diabetes," Dr. Lepper explained.

The study used data from 6,891 adults with CAP who were enrolled in the prospective CAPNETZ study from 2003 to 2009. Uni- and multivariable hazard ratios (HR) were adjusted for sex, age, body mass index, current smoking status, and CRB-65 (new onset of confusion; respiratory rate of 30 breaths/min or greater; systolic blood pressure of 90 mm Hg or less, or diastolic blood pressure of 60 mm Hg or less; and aged 65 years or older). CRB-65 is a clinical prediction rule that grades the severity of CAP in terms of 30-day mortality.

On multivariate analysis, it was determined that an elevated glucose level at hospital admission was an independent predictor of 28-, 90-, and 180-day mortality in CAP patients. In fact, increasing glucose levels corresponded to increasing risk for death from CAP. The study did not establish a causal relation between glucose levels and increased mortality risk in patients with CAP.

At the time of hospital admission, patients who had glucose levels from 6 to 11 mmol/l were considered to have mild acute hyperglycaemia and patients who had glucose levels of 14 mmol/l or more were considered to have acute hyperglycaemia. In all, 40% of CAP patients presented with hyperglycaemia. The majority (62%) of the patients were male, and average age was 60 years.

Patients with mild to moderate hyperglycaemia had a significantly higher HR for mortality at 90 days (1.55; 95% confidence interval: 1.18–2.04; P<.001) than patients with normal glucose levels at hospital admission. In patients presenting with acute hyperglycaemia, the HR increased to 6.04 (95% confidence interval: 4.18–8.74; P<.001).

"CAPNETZ is the largest trial to look at hyperglycemia as an independent risk factor for increased risk of death from pneumonia," said Dr. Lepper.

The CAPNETZ study was funded by the German Ministry of Education and Research, BundesministeriumfürBildung und Forschung.

www.medscape.com

Early. Check. Easy. Check.

Introducing the first real advance in acute kidney injury testing in more than 60 years, the NEPHROCHECK™ Test by Astute Medical. Unlike traditional renal tests that can take hours or days to provide results, these revolutionary, never-before-seen, early-rising biomarkers provide specific, accurate results in just minutes.

For details, visit CheckAKIRisk.com.

ASTUTE MEDICAL™

Innovative biomarkers. Smarter healthcare.

SEX IN THE ICU: ELIMINATING GENDER-BASED DISPARITIES IN CARE

Jennifer Innis, *NP, MA*

Lawrence S. Bloomberg Faculty of Nursing
Institute of Health Policy, Management and Evaluation
University of Toronto
Toronto, Ontario

Arlene S. Bierman, *MD, MS*

Keenan Research Centre
Li Ka Shing Knowledge Institute
St. Michael's Hospital
Lawrence S. Bloomberg Faculty of Nursing
Department of Medicine
University of Toronto
Toronto, Ontario

Arlene.Bierman@utoronto.ca

The time has come to apply a sex and gender lens to quality improvement in ICU care, considering not just biological differences but also potential gender bias from decision makers, among other factors. The authors of this article explore the current context of quality standards and indicators, and assess how access, quality and outcomes across genders can be optimised.

Introduction

Great strides have been made throughout Europe and North America in improving the quality and outcomes of care in the intensive care unit (ICU). Quality improvement interventions, including the use of care bundles, have increased adherence to evidence-based guidelines for ICU care. Meanwhile, validated quality indicators—for example, rates of ventilator-associated pneumonia (VAP) and central venous catheter-related bloodstream infections—facilitate measuring and monitoring improvement in critical care settings (McMillan et al. 2007). The European Society of Intensive Care Medicine (ESICM) has released a set of consensus indicators assessing structure, process and outcomes of ICU care, to be used in improving the safety and quality of care provided to critically ill patients (Rhodes et al. 2012), whereas in the US, quality indicators relevant to ICU care have been endorsed by the National Quality Forum (National Quality Forum, 2003).

Indicators of ICU care have also become the focus of attention of regulatory bodies seeking to contain costs and improve quality and safety of hospital care. Some of these efforts have been controversial. (Pronovost et al. 2008)

In the US, indicators of ICU care have been included in accreditation standards of the Joint Commission on Accreditation of Healthcare (JCAHO, 2005). In Ontario, Canada, rates of VAP and central-line infections are publicly reported with the goal of encouraging hospitals to reduce often-avoidable complications (Ministry of Health and Long-Term Care, 2012). Performance on indicators of ICU care have been linked to financial incentives in the US and the UK. Since 2008, with Medicare as the payer in the US, hospitals have no longer been reimbursed for care related to a list of "preventable" complications (Centers of Medicare and Medicaid Services, 2007). In the UK, in 2008, the Commissioning for Quality and Innovation payment system (CQUIN) was introduced to link payment to hospitals with good performance (Department of Health, 2008).

The Role of Sex and Gender

At the same time there is a growing body of literature on important sex- and gender-based differences related to critical care (Table 1),which could help to improve healthcare and patient outcomes.

In this article, we define "sex-based differences" as biological differences which may influence disease patterns and responses to treatment, while "gender differences" relate to the social context, which influences health, social and economic resources, as well as access to and experiences with care. Animal studies have found sex-based differences in immune response, and clinical studies have suggested sex-based differences in sepsis in-

> *"Presently, increased awareness of gender differences, routine sex stratification of quality indicators, and gender sensitive approaches to clinical decision making can all help increase gender equity in the ICU"*

cidence and response among critically ill patients (Fowler et al. 2009). Multiple studies have found gender-based disparities in ICU admission rates and care delivery patterns.

In other areas of medicine too, sex and gender differences in health and healthcare have been the focus of much attention. For example, sex-specific recommendations are included in many guidelines for the management of cardiovascular disease, while gender-based disparities in performance on widely used quality indicators for the management of ischemic heart disease and its risk factors have been well documented (Mosca et al. 2011). However, much less attention has been paid to addressing identified sex and gender disparities in ICU care.

Table 1. Sex and Gender Differences Related to ICU Care

Biology	Sex differences in disease prevalence and immune response
Diagnosis	Women are more often admitted with medical diagnosis and have higher rates of ARDS after critical injury, while men are more often admitted post elective surgery.
ICU Stays	Studies indicate higher rates of ICU admission for men, while women have a higher severity of illness on admission and shorter lengths of stay in the ICU.
Interventions	Women are less likely to receive common interventions including mechanical ventilation, pulmonary artery catheterisation, and central venous catheter insertion.
Health Outcomes	Women are at lower risk of contracting VAP. The literature on sex differences in mortality after ICU admission is mixed.
Research	Women are often under-represented in critical care research.

Gender-Based Disparities in Care

Gender disparities in ICU admission have been observed in both Europe and North America. Studies from Canada, Finland and Austria found that after controlling for illness severity, women were less likely to be admitted to an ICU than men (Fowler et al. 2007; Reinikainen et al. 2005; Valentin et al. 2003). Women have also been found to have a higher severity of illness on admission and shorter lengths of stay in the ICU than men (Valentin et al. 2003; Reinikainen et al. 2005; Vezzani et al. 2011). Older women appear to be at the highest risk for being denied ICU care. After controlling for potential confounders, Fowler and colleagues found that women over 50 years of age were not only less likely than men in the same age category to be admitted to an ICU, but also had higher rates of mortality (Fowler et al. 2007).

Women and men also differ in ICU admission diagnoses. It has been found that most often women are admitted with a medical diagnosis and men following elective surgery (Fowler et al. 2007). Furthermore, following acute traumatic injury, women have been found to develop higher rates of acute respiratory distress syndrome (ARDS) than men (Heffernan et al. 2011).

Once admitted to the ICU, there is evidence that female patients receive fewer interventions compared with male patients. Several large studies have found that female patients received fewer invasive procedures, including mechanical ventilation, pulmonary artery catheterisation, vasoactive medication use, and central venous catheter insertion than male patients, despite having the same or higher severity of illness (Fowler et al. 2007; Raine et al. 2002: Valentin et al. 2003).

> *"There appears to be an interaction between sex and age, with studies showing older women to be at particular risk for less aggressive care and suboptimal outcomes"*

Sex-Based Differences in Critical Illness

Sex-based differences in ICU outcomes, including mortality, have been found in multiple studies. However, findings have varied across studies, dependent on the condition and age of patients, with some studies finding a disadvantage for men, some for women, and some finding no sex-based differences. (Fowler et al. 2007; Frink et al. 2007; Reinikainen et al. 2005; Sperry et al. 2008). A French study found that among patients who develop hospital-acquired infections in the ICU, female gender is associated with higher mortality (Combes et al. 2009). Male sex was found to be an independent risk factor for VAP (Zahar et al, 2009). Table 1 offers a summary of sex- and gender-based differences in intensive care.

Factors Contributing to Sex- and Gender-Based Differences in Critical Care

Multiple factors may contribute to sex- and gender-based differences in critical

care (Bierman 2007):

1. Biology likely plays a role, as genetic factors and sex hormones may contribute to these differences. Recent studies have concluded that sex hormones influence response to stress and injury (Berry et al. 2009; Heffernan et al. 2011; Mohr et al. 2010);
2. Disease prevalence differs by sex, which influences admission diagnoses;
3. Women tend to have higher levels of comorbidity and disability, which can influence both clinical decision making and health outcomes;
4. There appears to be an interaction between sex and age, with studies showing older women to be at particular risk for less aggressive care and suboptimal outcomes;
5. Differences in decision making by physicians, patients and their caregivers may also contribute;
6. Gender bias, which has been shown to contribute to gender-based differences in cardiovascular care and orthopedic surgery, may also play a role. This bias may sometimes also lead to overuse of invasive procedures in men; and
7. The under-representation of women in clinical trials in the field of critical care has resulted in lacking evidence as to when gender-specific approaches may be needed.

Eliminating Gender- Based Disparities in Intensive Care

There is a lot that can be done to address sex- and gender-based differences in ICU care. Quality improvement initiatives can play an important role in fostering gender equity in critical care. Standardised guidelines and care bundles are widely used tools to support improved performance on quality indicators, including rates of VAP, central line infections, and venous thrombo-embolic events (McMillan et al. 2007). Use of guidelines to increase adherence to evidence-based practice recommendations can help ensure that both women and men receive indicated care. However, we will not know whether quality improvement activities reduce or eliminate gender-based disparities in ICU care unless quality indicators are sex stratified. Doing so, will provide a better understanding of gender differences in critical care as well as the impact of specific interventions on disparities.

Conclusion

Equity is an important dimension of healthcare quality (Bierman et al. 2012; Bierman and Clark 2007). In the future, advances in our understanding of sex differences relevant to critical care through both animal studies and increased representation of women in clinical trials may lead to sex-specific recommendations and guidelines. Presently, increased awareness of gender differences, routine sex stratification of quality indicators, and gender-sensitive approaches to clinical decision making can all help increase gender equity in the ICU.

The growing focus on ICU quality provides a great opportunity to reduce and in due course eliminate gender disparities in care. Ultimately, the goal is to optimise access, quality and outcomes of care for both woman and men in the ICU, delivering the right care, in the right setting, at the right time, to all patients. ■

References

Berry C et al. (2009). The effect of gender on patients with moderate to severe head injuries. J Trauma, 67, 950-953.

Bierman AS (2007). Sex matters: Gender disparities in quality and outcomes of care. CMAJ, 177, 1520-1521.

Bierman AS and Clark JP (2007). Performance measurement and equity. BMJ, 334, 1333-1334.

Bierman AS et al. (2012). Achieving health equity in Ontario: Opportunities for intervention and improvement. In: Bierman AS, editor. Project for Ontario Women's Health Evidence-Based Report: Volume 2: Toronto.

Centers of Medicare and Medicaid Services (2007). Medicare program: Changes to the hospital inpatient prospective payment systems and fiscal year 2008 rates, final rule, 72. Fed Regist, 72, 4129-8175.

Combes A et al. (2009). Gender impact on the outcomes of critically ill patients with noscomial infections. Crit Care Med, 37, 2506-2511.

Department of Health. Topic: Commissioning for Quality and Innovation payment system. www.dh.gov.uk, accessed August 2012.

Frink M et al. (2007). Influence of sex and age on MODS and cytokines after multiple injuries. Shock, 27, 151-156.

Fowler RA et al. (2009). Sex and critical illness. Curr Opin Crit Care, 15, 442-449.

Fowler RA et al. (2007). Sex- and age-based differences in the delivery and outcomes of critical care. CMAJ, 177, 1513-1519.

Heffernan DS et al. (2011). Gender and acute respiratory distress syndrome in critically injured adults: A prospective study. J Trauma, 71, 878-885.

Joint Commission on Accreditation of Healthcare Organizations (2005). Performance measurement in healthcare. www.jcaho.org. Accessed August 2012.

Ministry of Health and Long Term Care (2012). Patient Safety. Accessed August 2012

McMillan TR and Hyzy RC (2007). Bringing quality improvement into the intensive care unit. Crit Care Med, 35(Suppl.): S59-S65.

Mohr AM et al. (2010). Gender differences in glucose variability after severe trauma. Am Surg, 76, 896-902.

Mosca L et al (2011). Effectiveness-based guidelines for the prevention of cardiovascular disease in women – 2011 update: A guideline from the American Heart Association. Circulation, 123, 1243-1262.

National Quality Forum (2003). Safe practices for better healthcare: A consensus report. www.qualityforum.org. Accessed August 2012.

Pronovost PJ et al. (2008). The wisdom and justice of not paying for "preventable complications." JAMA, 299, 2197-2199.

Raine R et al. (2002). Influence of patient gender on admission to intensive care. J of Epidemiol Community Health, 56, 418-423.

Reinikainen M et al. (2005). Impact of gender on treatment and outcome of ICU patients. Acta Anaesthesiol Scand, 49, 984-990.

Rhodes A et al. (2012). Prospectively defined indicators to improve the safety and quality of care for critically ill patients: A report from the Task Force on Safety and Quality of the European Society of Intensive Care Medicine (ESICM). Intensive Care Med, 38, 598-605.

Sperry JL et al. (2008). Characterization of the gender dimorphism after injury and hemorrhagic shock: Are hormonal differences responsible? Crit Care Med, 36, 1838-1845.

Thijs LG, Members of the Task Force, European Society of Intensive Care Medicine (1997). Continuous quality improvement in the ICU: General guidelines. Intensive Care Med, 23, 125-127.

Valentin A et al. (2003). Gender-related differences in critical care: A multiple-center cohort study of therapeutic interventions and outcome in critically ill patients. Crit Care Med, 31, 1901-1907.

Vezzani A et al. (2011). Gender differences in case mix and outcome of critically ill patients. Gender Med, 8, 32-39.

Zahar J et al. (2009). Predicting the risk of documented ventilator-associated pneumonia: Construction and validation of a score. Crit Care Med, 37, 2545-2551.

Intelligent Ventilation solution from ICU to MRI

The **HAMILTON-MR1** ventilator provides maximum flexibility when transporting your adult or pediatric patients from the ICU to the MRI. The integrated gauss-meter, TeslaSpy, helps navigate through the magnetic field to allow you to position the ventilator safely as close as 1m to the MRI scanner (3T). The full featured HAMILTON-MR1 supplies all advanced modes of ventilation and offers outstanding non-invasive performance in a compact size. HAMILTON's patient oriented Adaptive Support Ventilation (ASV) and our unique Ventilation Cockpit supports you with the tools to achieve optimal patient care throughout the MRI procedure.

More information: www.hamilton-medical.com/MR1

HAMILTON MEDICAL AG
Via Crusch 8, CH-7402 Bonaduz, Switzerland
(+41) 81 660 60 10 (+41) 81 660 60 20
www.hamilton-medical.com
info@hamilton-medical.com

HAMILTON MEDICAL

END OF EMANCIPATION: UNRAVELLING THE EFFECT OF GENDER ON ICU MORTALITY

Irit Nachtigall, *MD*

Sascha Tafelski, *MD*

Maxim Kartachov, *MD*

Claudia Spies, *MD*

claudia.spies@charite.de

Department of Anaesthesiology and Intensive Care
Charité University Hospital Campus Charité Mitte and Campus Virchow-Klinikum
Berlin, Germany

Introduction

Debates have long existed on whether gender might either impact intensive care unit (ICU) outcome in general or only in distinct patient populations. Studies have enrolled patients without regard for a balance of gender distribution; hence, results mainly based on male patients have been used for females similarly.

> "In past years, studies in intensive care have revealed very conflicting results regarding gender-related effects on outcome"

One of the first sets of data that emphasised relevant differences between genders described patients with acute coronary syndrome. Goldberg et al. showed that female patients presented with different symptoms in the initial phase of acute myocardial infarction (Goldberg et al. 1998). Furthermore, evidence was provided that showed that discrepancies in initial presentation led to differences in clinical outcome (Srichaiveth et al. 2007). These and other results led to the conclusion that there is a strong need to assess gender effects to avoid possible differences in care processes provided and in outcomes from therapeutic measures. Consequently, this raised a first question that only seems to be answered simply.

Is there a Clinical Outcome Difference Between Genders in the ICU?

In past years, studies in intensive care have revealed very conflicting results regarding gender-related effects on outcome. Some authors have found female gender to be associated with lower ICU mortality (Ayanian and Epstein 1991; Adrie et al. 2007), some have described equal outcome (Crabtree et al. 1999; Wichmann et al. 2000) and others have shown significant associations between female gender and increased ICU mortality (Seymour et al. 2010; Vincent et al. 2006; Mercado-Martinez et al. 2010).

For the specific subgroup of patients with infections, differences in outcome and course of sepsis between genders cause equally controversial discussions. A recent retrospective study from Mahmood and colleagues showed that in a sample of more than 250,000 ICU patients in the US, female gender was associated with lower mortality when comparing patients under 50 years of age with an adjusted odds ratio (OR) of 0.83 (95% confidence interval: 0.76–0.91) (Mahmood et al. 2012). The subset of patients older than 50 years showed a different picture, however. Here, no difference in mortality was found (adjusted OR: 1.02, 95% confidence interval: 0.98–1.06). Interestingly, for patients admitted with sepsis there was a trend for higher mortality in females, but this difference was not of a significant level (adjusted OR: 1.07, 95% confidence interval: 0.99–1.16, P=0.08). Unfortunately, no data is provided for the subset of older females with sepsis as age was found to interact with results.

Our own prospectively collected data evaluated 709 mainly elderly patients and demonstrated that gender does not influence mortality in the main ICU population. However, in the analysis of the subset of patients with sepsis, female gender was significantly associated with fatal outcome, with an OR of 1.966 (95% confidence interval: 1.045–3.701, P=0.036) (Nachtigall et al. 2011). We were able to demonstrate that males were more likely to suffer from infection during ICU stay but that females had a relevant risk factor for dying with an infection. Table 1 provides a summary of study findings that show a link between female gender and mortality.

Pathophysiology Traces

One of the hypotheses that tries to explain the underlying pathophysiology is related to sex hormone differences, with etiology immune modulatory effects by female steroid hormones discussed. Depending on the hormone levels, oestrogen can be immune reinforcing or even anti-inflammatory. Oestradiol blocks proinflammatory tumor necrosis factor (TNF), interleukin (IL)-1 and IL-6 and, stimulates inhibitory IL-4 and IL-10. In healthy conditions, especially at preg-

HAMILTON·C3

Intelligent Ventilation

Visit us at ESICM Lisbon booth no. 23

ASV

Adaptive support ventilation.

The big picture in Intelligent Ventilation

The new HAMILTON-C3 has been designed to ventilate adult and pediatric patients in the critical care environment. With optional support, the HAMILTON-C3 is also able to ventilate infants and neonates.

The unique Ventilation Cockpit™, with its 12,1" high definition widescreen, provides exactly the information you need and helps you focus on what's important. The Dynamic Lung and the Vent Status window assist you in immediately identifying the patient's lung condition and assessing the weaning process. Adaptive Support Ventilation (ASV) makes ventilation intelligent by providing optimal support at each breath for virtually all patients.

The HAMILTON-C3 with built in batteries and a turbine give you maximum independence and flexibility to accompany your patient everywhere.

HAMILTON MEDICAL AG
Via Crusch 8, CH-7402 Bonaduz, Switzerland
Tel (+41) 81 660 60 10 Fax (+41) 81 660 60 20
www.hamilton-medical.com

HAMILTON MEDICAL

Table 1. Selected Clinical Studies Evaluating Impact of Female Gender on Mortality and Derived Odds Ratios Giving Risk for Female Patient Death Compared to Men

Study	Population/ Measure	Odds Ratio Giving Risk for Female Patient Death Compared to Men (95% Confidence Interval)
Adrie et al. (2007). Chest. Matched cohort N= 1692	Severe sepsis / hospital mortality	0.75 (0.57 - 0.97) p = 0.02 overall population 0.69 (0.52 - 0.93) p = 0.014; >50 years 1.01 (0.52 - 1.97) p = 0.98; <50 years
Crabtree et al. (1999). JAMA. Observational cohort N= 892	Surgical wards, patients with infections / hospital mortality	1.32 (0.90 -1.94); p = 0.16 overall population 2.25 (1.17 - 4.32) p = 0.02 pneumonia
Vincent et al. (2006). CCM. Multicenter observation N= 1177	Sepsis / ICU mortality	1.4; (1.1 – 1.8) p = 0.013
Mercado-Martínez (2010). ICM. Multicenter observation N= 6,458	Acute coronary syndrome / ICU mortality	1.64 (1.29 - 2.09)
Mahmood et al. (2012). Crit Care. Multicenter observation ; N= 261255	ICU patients / ICU mortality	0.83 (0.76 - 0.91); overall age <50 1.02 (0.98 - 1.06); overall age >50
Nachtigall et al. (2011). Crit Care. Observational cohort, N=709	ICU patients / ICU mortality	1.277 (0.720-2.264) P=0.403; overall 1.909 (1.002-3.638) p=0.049, Sepsis subgroup
Combes et al. (2009). Crit Care Med. Observational cohort study N= 1341	ICU patients with infections / ICU mortality	1.50 (1.11 - 2.03)
McGwinn et al. (2002). Shock Observational cohort N= 1611	Burn injury patients / ICU mortality	2.3 (1.4-3.8) < 60 years 0.9 (0.5-1.6) > 60 years
Magnotti et al. (2008). J.Am.Coll.Surg Trauma registry study; N=35706	Trauma patients / hospital mortality	1.044 (0.912 – 1.196) p = 0.53

nancy level, oestrogen enhances nitric oxide (NO) production by stimulating the expression and activity of different isoforms of nitric oxide synthetase (NOS). In contrast, in the presence of lipopolysaccharide (LPS), oestrogen blocks the inducible NOS and consequently the NO production. Furthermore, oestrogen inhibits the formation of oxygen radicals and apoptosis. On the postmenopausal level, oestradiol, stimulates TNF, interferon (INF)-γ and IL-1β (Straub 2007).

In animal studies, there seems to be consistency in the positive effect of oestrogen on sepsis and shock caused by trauma. In haemorrhagic shock and sepsis, female animals show less immune suppression, higher IL-3 and IL-1 levels, and better chances of survival than their male counterparts (Wichmann et al. 2000; Zellweger et al. 1997; Diodato et al. 2001). This effect correlates with the 17β-oestradiol level in the female cycle (Knoferl et al. 2001). Ovariectomised animals lose this advantage over male animals, but this can be recovered by administration of 17β-oestradiol (Knoferl et al. 2001; Jarrar et al. 2000). Oestrogen substitution can also support the hepatic and cardiac function of male animals with haemorrhagic shock (Mizushima et al. 2000). Furthermore, a blockade of the testosterone receptors reestablishes the immune function and attenuates the liberation of IL-1 and IL-2, thus impeding the induction of sepsis and enhancing survival (Angele et al. 1997; Mizushima et al. 2000) .

Clinical Data to Support Experimental Results

In clinical studies, experimental results could not be clearly reproduced, and so far no conclusive evidence can be found. Schroder and his team were able to show, in a study on 52 septic patients, that women had a better outcome, lower TNF-α and higher IL-10 level (Schroder et al. 1998). Some years later, Adrie and colleagues examined 1,692 patients with severe sepsis and found that women had a lower rate of central venous catheter

use, fewer days on a ventilator, a shorter length of stay on ICU and lower mortality (Adrie et al. 2007).

Offner and associates identified male gender as one risk factor for postoperative infections (Offner et al. 1999), while, in contrast, Eachempati and colleagues found a higher mortality in female patients with sepsis in the US (Eachempati et al. 1999). Similar results were found in a European multi-centre study involving 3,147 patients with sepsis (Vincent et al. 2006). Combes and his team retrospectively evaluated more than 1,300 patients with nosocomial infections in a mixed ICU and found an increased risk of death with excess mortality of five percent and an adjusted odds ratio (OR) of 1.50 (95% Confidence Interval: 1.11-2.03) for female gender (Combes et al. 2009). Other studies showed higher mortality for women with blunt abdominal trauma (Napolitano et al. 2001), burns (McGwin et al. 2002) and sepsis caused by abdominal infection (McLauchlan et al. 1995).

In opposition, there are studies showing no correlation between gender and mortality (Oberholzer et al. 2000; Magnotti et al. 2008; Angus et al. 2001). Based on natural scientific understanding, there should be an explanation for these contradictory results.

Transferability of Experimental Data

Direct translation from bench to bedside seems difficult. Experimental sepsis is short in comparison with the clinical course of sepsis in humans, and the animals involved are younger without comorbidities. Furthermore, in the experimental setting, the onset of sepsis can be tailored to the hormonal status, so most studies are conducted when oestrogen levels are highest. Besides this, animal studies control the surroundings, possibly biasing the results, and there is no gender-based difference in treatment intensity in animal experiments.

Summarising the principle concerns regarding the transferability of the experimental setting on the one hand and the clinical impact of gender as one variable in the complex clinical setting of ICU care on the other hand, there remain concerns, and another hypothesis has been addressed.

Another Hypothesis to Explain Gender Differences

Another hypothesis is related to a difference in healthcare allocation between genders, based on clinical data. Valentin and colleagues found via a large observational cohort study of ICU patients that men received more invasive procedures like mechanical ventilation, central venous or pulmonary artery catheterisation, catecholamine and kidney replacement therapy (Valentin et al. 2003). Although increased overall mortality in female patients was observed, severity of illness-adjusted mortality rate was not different in this study. Thus, the authors conclude that different therapeutic approaches in male patients are not translated into survival advantages. Another study in an emergency department focused on factors for non-adherence to early goal-directed therapy. In this setting, Mikkelsen and associates demonstrated that it was less likely for females to receive this therapy; the probability was further reduced when the physician in charge was also female (Mikkelsen et al. 2010). Han and colleagues observed low adherence rates for lung protective ventilation measures in females, conceivably because of their smaller stature (Han et al. 2011).

To evaluate this allocation factor we also analysed possible gender-related effects in healthcare distribution and focused on the quality of infection diagnostics and antibiotic therapy. For both, in the general postoperative cohort study as well as the subgroup of patients with sepsis, no relevant difference regarding quality of care was found (Nachtigall et al. 2011). There seems to be a trend for a more strict indication of diagnostic procedures with exposure to radiation in females. This difference might be attributed to the intention to limit possible risks for the ovules. Of course, possible misallocation of therapeutic measures should be monitored closely, but currently there is no precise evidence that any existing slight difference of care for female patients would impact ICU outcome.

Differences in Physiology

Besides differences in anthropometric indices, female patients show some specific differences compared to males. Women have a different distribution volume than men, meaning an altered effect duration and elimination of medical agents used on ICUs. Examples for this effect are seen in the use of midazolam and vancomycin (Greenblatt et al. 1984; Ducharme et al. 1994).

Other examples of differences in metabolism can be found regarding the CYP-450 system with clinical relevance. Females show a faster elimination of methylprednisolone while they are more sensitive to the drug itself (Lew et al. 1993). A differing sensitivity of receptors may explain the disparity in the effect of morphine between genders and why propofol-based general anaesthesia is faster degraded in female

> *"For the specific subgroup of patients with infections, differences in outcome and course of sepsis between genders cause equally controversial discussions"*

patients (Dahan et al. 1998; Gan et al. 1999). Furthermore, there is evidence that sex hormones interact with pharmaceuticals, for example, hormone-induced QT prolongation, having consequent effects on cardioactive medicine and potentially causing adverse drug reactions (Rodriguez et al. 2001). In the field of gender-specific influences on medication, lots of question marks remain, emphasising the need for balanced cohort studies to assess the effectiveness and safety of established and new drugs.

Different Physiology; Same Scores?

Facing all those differences in physiology, it does not seem to be reasonable to assess sepsis in both genders with the same measurements, and the use of the same intensive care scoring systems may be questioned. The Acute Physiology And Chronic Health Evaluation (APACHE) and the Sequential Organ Failure Assessment (SOFA) methods integrate laboratory and physiological items regardless of the specific limits in both genders, whereas the score performance should be different. Using the same scoring items could lead to a bias concerning the severity of disease, and sepsis might be misstratified. Summarising this, it might be desirable to adopt gender-specific scores and to use gender-related corrections like the Framingham-score (Wilson et al. 1998) or the CHA2DS2-VASc-score in cardiology (Lip et al. 2010).

Conclusion

Gender has been shown to be outcome relevant in the ICU setting. Through consequent considerations from clinical studies, gender is one relevant factor for future evidence-based decision making. Currently, gender-related impacts of medical interventions and drug therapy undergo intensive evaluation, and the results of these studies will influence therapy recommendations in future, even gender-specific guidelines could be on the horizon. It is expected that a more detailed understanding of differences in clinical presentation, course of diseases and cure processes will support a better knowledge of underlying pathophysiology. ■

References

Adrie C et al. (2007). Influence of gender on the outcome of severe sepsis: a reappraisal. Chest 132:1786-1793.

Han S et al. (2011). Short women with severe sepsis-related acute lung injury receive lung protective ventilation less frequently: an observational cohort study. Crit Care 15:R262.

Jarrar D et al. (2000). The female reproductive cycle is an important variable in the response to trauma-hemorrhage. Am.J.Physiol Heart Circ.Physiol 279:H1015-H1021.

Magnotti LJ et al. (2008). Impact of gender on outcomes after blunt injury: a definitive analysis of more than 36,000 trauma patients. J.Am.Coll.Surg. 206:984-991.

Mahmood K et al. (2012). Association of gender with outcomes in critically ill patients. Crit Care 16:R92.

McGwin G et al. (2002). Gender differences in mortality following burn injury. Shock 18:311-315.

Nachtigall I et al. (2011). Gender-related outcome difference is related to course of sepsis on mixed ICUs: a prospective, observational clinical study. Crit Care 15:R151.

Napolitano LM et al. (2001). Gender differences in adverse outcomes after blunt trauma. J Trauma 50:274-280.

Oberholzer A et al. (2000). Incidence of septic complications and multiple organ failure in severely injured patients is sex specific. J.Trauma 48:932-937.

Seymour CW et al. (2010). Marital status and the epidemiology and outcomes of sepsis. Chest.

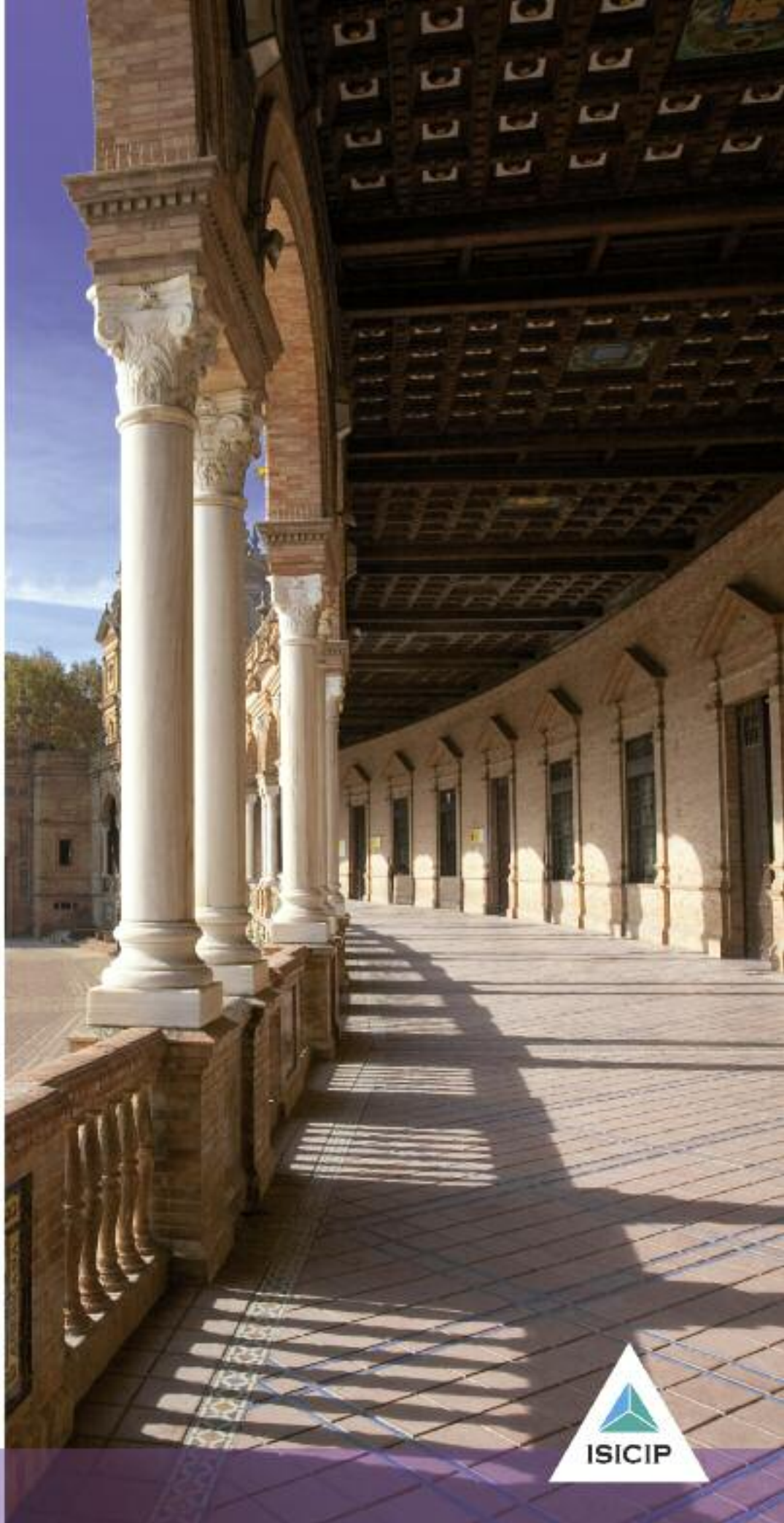
Straub RH (2007). The complex role of estrogens in inflammation. Endocr.Rev. 28:521-574.

Vincent JL et al. (2006). Sepsis in European intensive care units: results of the SOAP study. Crit Care Med 34:344-353.

For full references, please send a request to **editorial@icu-management.org**

18th International Symposium on Infections in the Critically ill Patient

Sevilla
7-8 February
2013



The aim of this two days symposium is to review current concepts, technology and present advances in infections in the critically ill patients.

Sepsis, Pulmonary Infections, Basic Research, Pulmonary Infections Treatment and Prophylaxis Therapy of severe infections will be the topics of the main sessions presented by experts who will review and update the new advances on infections in the critically ill patient. At the end of each session a Clinical Controversy, Pannel Discussion or Case Report Discussion will be organized.

Organized by

Antonio Artigas, MD
Jean Carlet, MD
Michael Niederman, MD
José Garnacho, MD

ISICIP

www.infections-online.es

OPTIMAL NUTRITION IN INTENSIVE CARE: DOES GENDER MATTER?

Sandra N. Stapel, *MD*

Department of Intensive Care Medicine
VU University Medical Center
Amsterdam, The Netherlands

s.stapel@vumc.nl

Peter J.M. Weijs, *PhD*

Department of Intensive Care Medicine
Nutrition and Dietetics
VU University Medical Center
Nutrition and Dietetics
Amsterdam University of applied sciences
Amsterdam, The Netherlands

Armand R.J. Girbes, *MD, PhD*

Department of Intensive Care Medicine
VU University Medical Center
Amsterdam, The Netherlands

Albertus Beishuizen , *MD, PhD*

Department of Intensive Care Medicine
VU University Medical Center
Amsterdam, The Netherlands

Several gender differences relate to optimal nutrition in intensive care. We describe these differences and their hypothetical implications for the patient.

Introduction

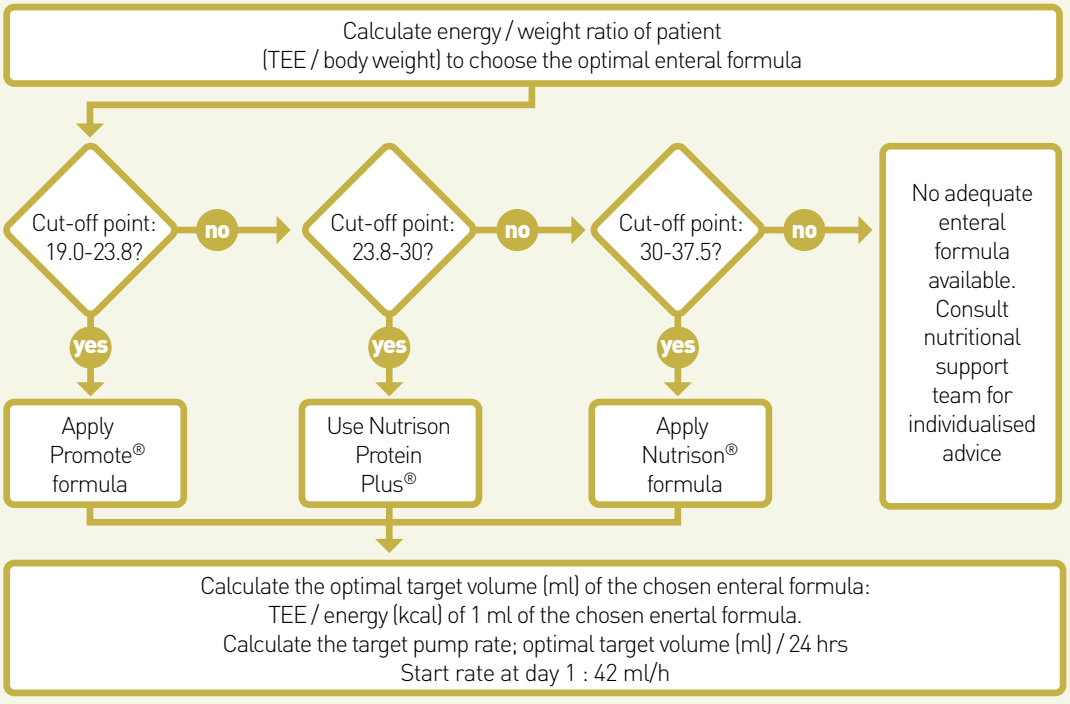
Nutrition therapy is an integral and important part of therapy in the intensive care unit (ICU). Malnutrition leads to more complications, more infections, longer hospital stays and even death (Lochs 2006, Norman 2008). Maintenance of lean body mass is crucial to improve outcome in critical care; hence, nutrition therapy aims at conservation or restoration of the body protein mass and provision of adequate amounts of energy. In adult intensive care, we generally treat all our patients in a similar fashion, in spite of large differences in age, posture, race or gender. In particular, body composition differs substantially between males and females, as does rate of metabolism. In the concept of optimal nutrition of critically ill patients the primary aim is to target individual needs of energy and protein, incorporating various parameters such as body weight, length and gender (for example, when using energy expenditure formulas). However, what is the basis for a gender-specific nutritional strategy, and what is the potential effect of this approach on outcome?

Optimal Nutrition

The first of several challenges is that of defining optimal nutrition. Adequate nutrition in intensive care is defined as providing energy as measured by indirect calorimetry, with the amount of protein reaching at least 1.2 g/kg pre-admission body weight per day. (Sauerwein and Serlie 2010; Sauerwein and Strack van Schijndel 2007). However evidence supporting these nutritional goals is mainly based on surrogate outcome parameters.

Another well-known challenge is to attain optimal nutrition. We developed a nutrition algorithm to

Figure 1. Energy-Protein Algorithm Connecting the Mathematical Relation Between Energy-Protein Needs of Patients and the Energy-Protein Content of (Par)Enteral Formulae.



TEE: total energy expenditure

improve nutrition therapy, which is fully incorporated into a patient data management system (Strack van Schijndel 2007). This energy-protein algorithm connects the mathematical relation between energy-protein needs of patients and the energy-protein content of (par)enteral formulae. The algorithm provides an appropriate nutrition formula for each ICU patient and also provides adequate pump speed to reach prespecified protein and energy targets (Figure 1).

A third challenge is to show the benefit that nutrition strategies have on outcome. Most studies failed to demonstrate any impact on outcome (Barr J et al. 2004; Doig GS et al. 2008; Martin CM et al. 2004). We have investigated the effect of our energy-protein targeted approach on clinical outcome in mechanically ventilated critically ill patients in a prospective observational study (Strack van Schijndel et al. 2009; Weijs et al. 2012).

Benefit on Outcome for Females Only?

In a prospective observational cohort study of 243 patients in a mixed medico-surgical ICU, we surprisingly found that optimal nutritional therapy, defined as more than 90% of total energy expenditure as measured by indirect calorimetry and provision of 1.2–1.5 g of protein/kg per day, was associated with reduced ICU, 28-day, and hospital mortality in female patients only. Female patients for whom both energy and protein goals were reached had better outcomes than those for which only energy goals were reached.

For males, no benefit from optimal nutrition could be demonstrated. We could not explain this finding, but we speculated that females have a lower protein mass, largely manifested as muscle mass, and therefore may have had a larger benefit from optimal protein delivery. In a later extended analysis consisting of 886 patients (including the 243 patients mentioned above), we confirmed that optimal nutrition therapy in mechanically ventilated critically ill, defined as both protein and energy targets reached, was associated with a decrease in 28-day mortality by 50%; however, we found this effect in both male and female patients. The gender difference was lost in this larger trial.

Gender Related Differences in Nutrition

There are several gender differences that relate to nutrition and these differences come with several hypothetical implications. The metabolic rate of men is generally higher than in women, due to larger body size and mainly higher active cell mass. This is taken into account in the most commonly used energy expenditure formulae. Body composition differs substantially between males and females.

A possible explanation for the difference in effect of nutritional therapy between men and women might be that the maintenance of protein mass in the body above the critical minimum is vital to survival. In other words, a lean body mass above the critical level is essential for the human body to function in a vital manner. Beyond this hypothesised protein threshold, loss of organ function and failing immune status will contribute to mortality. If this hypothesis is true, males have an advantage in nutritional reserve, because they are heavier and also have a more favourable proportionality between fat and protein, with larger relative protein stores.

Females may have a disadvantage, because they will reach this presumed minimum protein threshold in a shorter period of time during catabolism. On the other hand, it is suggested that fat stores might "protect" protein stores during periods of underfeeding, which might benefit females. Adequate nutrition aims to protect the body composition and is aimed at slowing down net protein catabolism. Due to the smaller reserves that females have, the effect of nutrition will be more obvious. However, with the exception of our first analysis (Strack van Schijndel et al. 2009), no reported studies account a gender-specific effect on outcome from nutritional interventions.

Another important consideration is that the energy deficit occurs mainly in the first days after admission, when targeted volume cannot be administered for practical reasons, such as gastric retention, slow increase of nutrition towards the targeted volume, haemodynamic instability, and diagnostic and therapeutic interventions. Allowed gastric residual volume is similar in males and females whilst the amount of enteral feeding in ml/hour is generally lower for women because of smaller caloric and protein needs. This might contribute to females reaching nutritional goals earlier.

Conclusion

There is still much debate about whether gender plays a role in outcome in critical care. Studies evaluating this relationship in critically ill patients have reached inconsistent results. We believe that gender differences relate to optimal nutrition in intensive care and these differences come with several hypothetical implications. For studies that found a gender-related difference in outcome, it would be interesting to specifically look at whether nutritional targets were reached more often and earlier in women, especially in the first days after admission. ■

References

Barr J et al. (2004). Outcomes in critically ill patients before and after the implementation of an evidence-based nutritional management protocol. Chest,125:1446-1457.

Doig GS et al. (2008). Effects of evidence-based feeding guidelines on mortality of critically ill patients: a cluster randomized controlled trial. JAMA, 300:2731-2741.

Lochs H et al. (2006). Evidence supports nutritional support. Clin Nutr, 25:1779.

Martin CM et al. (2004). Multicentre, cluster-randomized clinical trial of algorithms for critical-care enteral and parenteral therapy (ACCEPT). CMAJ,170:197-204.

Norman K et al. (2008). Prognostic impact of disease related malnutrition. Clin Nutr 27:5-15.

Pichard C et al. (2004). Nutritional assessment: lean body mass depletion at hospital admission is associated with an increased length of stay. Am J Clin Nutr, 79:613.

Sauerwein HP and Serlie MJ (2010). Optimal nutrition and its potential effect on survival in critically ill patients. Neth J Med, 68:119-22.

Sauerwein HP and Strack van Schijndel RJM (2007). Perspective: How to evaluate studies on peri-operative nutrition? Considerations about the definition of optimal nutrition for patients and its key role in the comparison of the results of studies on nutritional intervention. Clin Nutr, 26:154-8.

Strack van Schijndel et al. (2007). An algorithm for balanced protein/energy provision in critically ill mechanically ventilated patients. E Spen Eur E J Clin Nutr Metab, 2: 69-74.

Strack van Schijndel RJM et al. (2009). Optimal nutrition during the period of mechanical ventilation decreases mortality in critically ill, long-term acute female patients: a prospective observational cohort study. Crit Care, 13:R132.

Weijs PJ et al. (2012). Optimal protein and energy nutrition decreases mortality in mechanically ventilated, critically ill patients: a prospective observational cohort study. JPEN, 36: 60-8.

Update on Nutritional Support

Rome, Italy
December 16-19, 2012

Management & coordination:
Véronique De Vlaeminck
Erasme University Hospital
Route de Lennik 808 – B-1070 Brussels
Email : veronique.de.vlaeminck@ulb.ac.be

www.intensive.org

Hôpital Erasme | ULB

PERIOPERATIVE NUTRITION IN UPPER GASTROINTESTINAL CANCER PATIENTS

Christophe Mariette, *MD, PhD*

Professor of Surgery
Department of Digestive and Oncological Surgery
University Hospital of Lille
Lille, France

christophe.mariette@chru-lille.fr

Malnutrition is frequently observed in upper gastrointestinal cancer surgical patients; it is an independent predictor of postoperative morbidity and mortality and leads to both increased length of hospital stay and hospital costs. Consequently, every effort should be made to apply nutritional support, including both standard enteral nutrition (EN) and immunonutrition, as a complementary therapeutic limb in current oncological treatment protocols.

Epidemiology and Consequences of Malnutrition

Gastric and oesophageal cancers are among the leading causes of cancer-related death worldwide due to late presentation and poor prognosis. In curable disease, a therapeutic strategy encompassing surgery, chemotherapy and/or chemoradiation is thus mandatory (Mariette et al. 2012). Malnutrition is frequently observed in 60–85% of surgical patients with an upper gastrointestinal cancer (Stratton et al. 2003) and is an independent predictor of postoperative morbidity and mortality, leading to increased length of hospital stay and hospital costs (Stratton et al. 2006). Many factors can affect nutritional status, particularly disease stage and the choice of treatment used (surgery, chemotherapy and/or radiotherapy) (Van Cutsem 2005). Nutritional support should therefore be used as a strong therapeutic weapon, which may be complementary to standard active oncological therapy.

Nutritional Interventions in Digestive Cancer Surgery

Nutritional support in oncology patients aims to prevent early death, decrease postoperative complications and improve quality of life. It should begin early and be a routine part of the treatment of cancer patients. Depending on patients' individual needs, these goals may be achieved by giving patients nutritional recommendations and dietary advice, as well as by providing artificial nutrition using oral supplements, EN via a feeding tube, or parenteral nutrition (PN).

Dietary advice may be sufficient when the patient is capable of consuming at least 75% of his or her nutritional requirements to maintain good health and there is no radiotherapy, chemotherapy or surgery scheduled. However, when these requirements are not met and dietary advice is insufficient, a higher level of nutritional support must be initiated. Oral supplementation should be used in cases of malnutrition or when the patient is unable to consume at least 50–75% of his or her requirements by means of conventional feeding for a period longer than five consecutive days.

In moderate or severe malnutrition, or when patients are unable to consume at least 50% of their requirements through conventional feeding for more than five consecutive days (Lipman 1998; Braunschweig et al. 2001), enteral feeding is required. The implementation of EN is recommended when the patient's gastrointestinal tract is functional as it appears to have better efficacy, lower cost and cause less iatrogenic complications than PN (Mariette et al. 2005). In cases where swallowing is affected, for example in oesophageal cancer, or if serious mucositis is expected, EN should be administered through a nasogastric or nasoenteric tube for a duration of two to three weeks. Alternatively, gastrostomy (in oesophageal cancer) and jejunostomy (in oesogastric cancer) feeding may be administered for a duration of more than two to three weeks (Mariette et al. 2005, Conference de consensus 1995). Figures 1 and 2 propose an algorithm for deciding upon the route of EN administration in oesophageal and gastric cancers, respectively. In a recent review of our experience with percutaneaous radiological gastrostomy (PRG) before surgery for oesophageal cancer, we found a PRG complication rate of 3.4%, without any incidence of metastatic inoculation and

> *"Routine immunonutrition may help to support immune and nutritional status during the neoadjuvant and perioperative treatment periods"*

without any injury of the gastric vascular arcade, thus not compromising subsequent gastric pull-up. Due to early enteral feeding, outcomes of malnourished patients were similar to those of non-malnourished patients (Tessier et al. 2012).

As other scientific societies have done, the French Society of Digestive Surgery established guidelines, graded from A to C (a grading system is summarised in Table 1), on perioperative nutritional support in GI cancer surgery (Mariette et al. 2005), including the following suggestions:

- During the perioperative period, EN is not required in well-nourished patients, those with weight loss of <10% or in patients who can sustain an oral diet providing at least 60% of their needs within the week following surgery (Grade A).
- Preoperative nutrition is recommended in severely malnourished patients with weight loss ≥20% who will undergo major surgery (Grade A). The same approach seems to be beneficial for patients with moderate malnutrition (weight loss of 10–19%) (Grade B).
- Postoperative nutrition is recommended:
  i. In all patients who benefited from preoperative nutrition (Grade A);
  ii. In all malnourished patients who did not benefit from preoperative nutrition (Grade A);
  iii. In patients who cannot resume an oral diet in the postoperative course due to surgical complications (Grade A), or in patients consuming <60% of the required diet within the week following surgery (Grade A); and
  iv. In other patients for whom no unequivocal recommendation could be drawn (Grade B).

Figure 1. Artificial Nutrition Strategy in Oesophageal Cancer Patients According to Percentage of Weight Loss

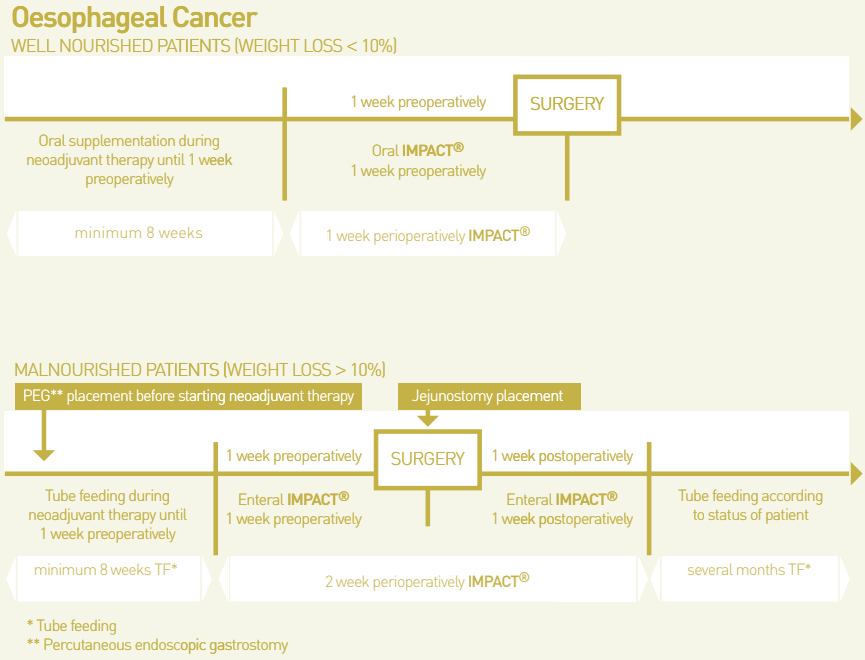
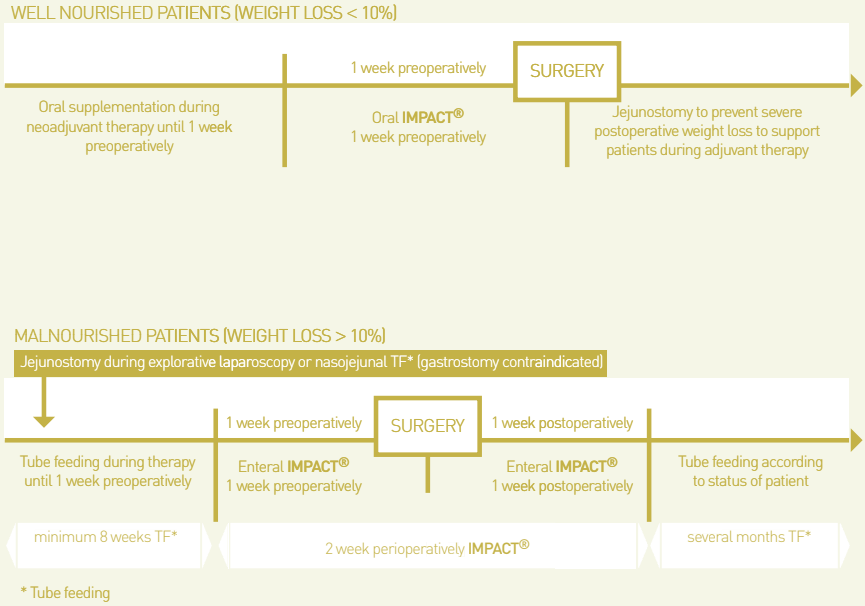


Figure 2. Artificial Nutrition Strategy in Gastric Cancer Patients According to Percentage of Weight Loss



Immunonutrition

Major surgery leads to a decline in immune status, and an increase in postoperative mortality and rates of infectious morbidity. Enhancing immune function could help decrease such complications. In recent years, standard EN has been enhanced with nutrients whose specific purpose is to up-regulate the host immune response, control the inflammatory response and improve nitrogen balance and protein synthesis following surgery. The immunonutrients used are glutamine, arginine, poly-unsaturated fatty acids (omega-3), nucleotides, taurine, vitamins A, E, and C, beta-carotene and trace elements.

The use of immunonutrition in the surgical setting has been well studied with over 28 randomised controlled trials

Table 1. Grading of Guidelines According to the French National Authority for Health (www.has-sante.fr)

Level of published scientific evidence	Grade of guidelines
Level 1: • Randomised controlled trials of high-power • Meta-analyses of randomised controlled trials • Decision analyses based on properly conducted studies	**Grade A** Established scientific evidence
Level 2: • Randomised controlled trials of low-power • Properly conducted non-randomised controlled studies • Cohort studies	**Grade B** Presumption of scientific evidence
Level 3: • Case-control studies	**Grade C** Low level of evidence
Level 4: • Comparative studies with major bias Retrospective studies Case series	

showing that immunonutrition is more efficient than standard isocaloric and isoenergetic nutrition in significantly decreasing postoperative infectious morbidity, length of hospital stay and healthcare costs (Gianotti et al. 2002, Beale et al. 1999).

However, there is a great degree of heterogeneity in terms of nutritional status and the type of control used, and in some studies samples were quite small. Despite this, the effect of immunonutrition has generally been found to be beneficial, especially in malnourished patients.

Numerous meta-analyses have assessed the evidence relating to the use of immunonutrition in the surgical setting (Cerantola et al. 2011; Marimuthu et al. 2012). The overall conclusion is that in surgical patients, a lower rate of infectious complications and shorter hospital stay were associated with perioperative immunonutrition, relative to standard EN.

Figure 3 illustrates a decision tree for the nutritional management of patients undergoing GI cancer surgery.

Enteral immunonutrition lasting five to seven days is recommended in the preoperative setting in all patients who will benefit from oncological GI surgery (Grade A). In the postoperative period, immunonutrition should be continued in all patients who were malnourished in the preoperative period:

- For five to seven days, provided that there are no postoperative complications; or
- Until patients can consume an oral diet meeting at least 60% of their requirements (Grade A).

> *"Gastric and oesophageal cancers are among the leading causes of cancer-related death worldwide due to late presentation and poor prognosis"*

Putting the Perspective into Practice

It is known that:

(i) Immunonutrition is efficient in the perioperative period in oesophago-gastric cancers;

(ii) Both oesophageal and gastric cancer patients are frequently malnourished; and

(iii) Most patients with oesophago-gastric cancer will receive neoadjuvant chemo(radio)therapy that may compromise both nutritional and immune status.

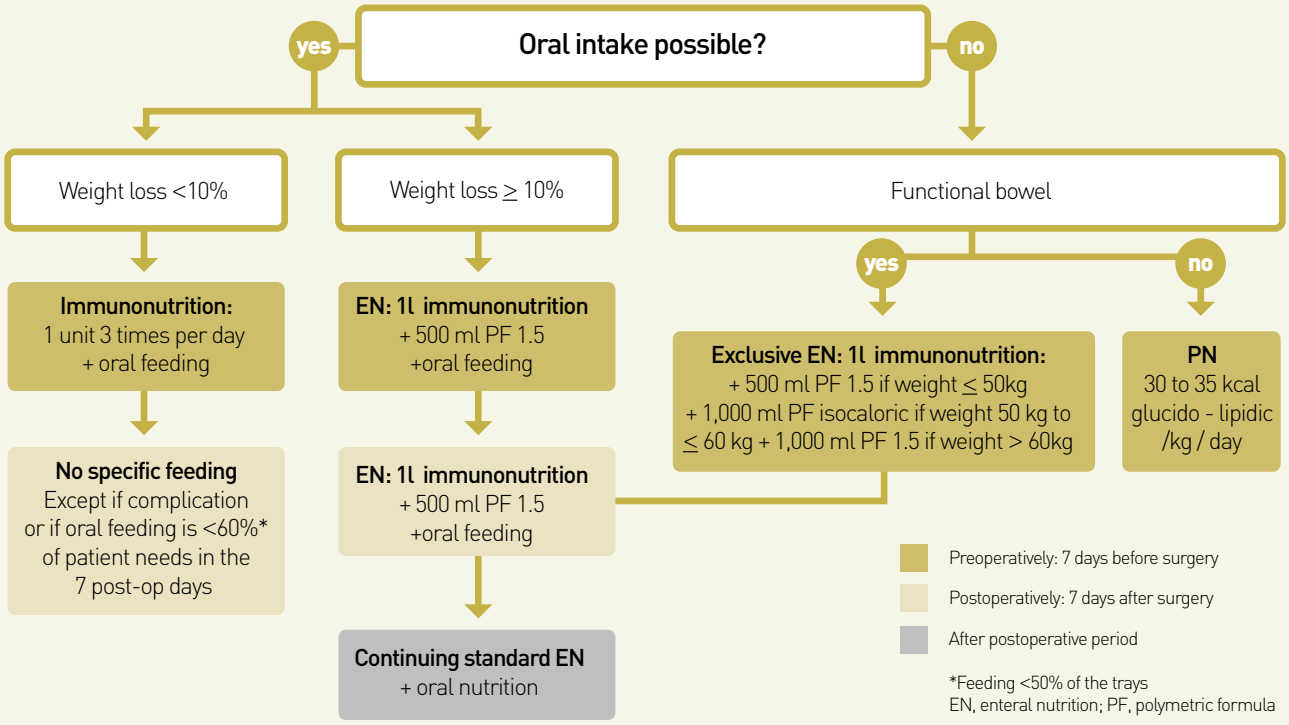
Hence, routine immunonutrition may help to support immune and nutritional status during the neoadjuvant and perioperative treatment periods. To test this hypothesis, an ongoing European randomised controlled trial sponsorised by NestléHealthScience, with myself Prof. Mariette as Principal Investigator, is assessing the role of long-term administration of immunonutrition during the neoadjuvant and the surgical phases to improve quality of life, to reduce postoperative morbidity and to reduce neoadjuvant treatment toxicities (NCT01423799).

Conclusion

Knowledge of the nutritional status of patients with oesophago-gastric cancer is essential, not only in identifying malnourished and non-malnourished patients, but also in allowing treatment adaptations along each step of the multimodal oncological treatment path. Whether or not the treat-

ment procedure is surgical, all patients could benefit from nutritional support during oncologic treatments. Preoperative immunonutrition lasting five to seven days is proposed for both malnourished and non-malnourished patients with oesophago-gastric cancer, along with artificial nutrition for at least seven days after surgery for malnourished patients. Dietary counselling should be provided to all patients receiving chemotherapy and/or radiotherapy. Surgeons play a key role in including and applying nutritional support as a strong therapeutic weapon in the oncological therapeutic strategy for GI cancer patients. ■

Figure 3. Nutritional Management of Patients Undergoing Surgery for GI Cancer



References

Beale RJ et al. (1999). Immunonutrition in the critically ill: a systematic review of clinical outcome. Crit Care Med. 27:2799-805.

Braunschweig CL et al. (2001). Enteral compared with parenteral nutrition: a meta-analysis. Am J Clin Nutr. 74:534-42.

Cerantola Y et al. (2011) Immunonutrition in gastrointestinal surgery. Br J Surg. 98:37-48.

Conference de consensus (1995). Nutrition péri-opératoire en chirurgie réglée de l'adulte. Nutr Clin Metabol. 9(suppl 1):1-50

Gianotti L et al. (2002). A randomized controlled trial of preoperative oral supplementation with a specialized diet in patients with gastrointestinal cancer. Gastroenterology.122:1763-70.

Lipman TO (1998). Grains or veins: is enteral nutrition really better than parenteral nutrition? A look at the evidence. JPEN J Parenter Enteral Nutr. 22:167-82.

Mariette C et al. (2012). Surgery in Esophageal and Gastric Cancer Patients: What is the Role for Nutrition Support in your Daily Practice? Ann Surg Oncol. 19:2128-34.

Mariette C et al. (2011). Oesophagogastric junction adenocarcinoma: which therapeutic approach?
Lancet Oncol. 12:296-305.

Mariette C et al. (2005). Société Française de Chirurgie Digestive. Perioperative care in digestive surgery. J Chir (Paris). 142:14-28.

Marimuthu K et al. (2012). A meta-analysis of the effect of combinations of immune modulating nutrients on outcome in patients undergoing major open gastrointestinal surgery. Ann Surg. 255:1060-8.

Stratton RJ and Elia M (2006). Deprivation linked to malnutrition risk and mortality in hospital. Br J Nutr. 96:870-6.

Stratton R, et al. (2003). Prevalence of disease-related malnutrition. In: Stratton RJ, Green CJ, Elia M, eds. Disease-related malnutrition: An evidence-based approach to treatment. CABI Publishing, Wallingford, Oxon. 35-92.

Tessier W et al. (2012). Percutaneous radiological gastrostomy in oesophageal cancer patients: a feasible and safe access for nutritional support during multimodal therapy. Surg Endosc. Sep 7. [Epub ahead of print]

Van Cutsem E and Arends J (2005). The causes and consequences of cancer-associated malnutrition. Eur J Oncol Nurs. 9 Suppl 2:S51-63.

IMPACT ON HOSPITAL COST OF USING IMMUNONUTRITION TO REDUCE RISK OF COMPLICATIONS IN CANCER PATIENTS UNDERGOING MAJOR GASTROINTESTINAL SURGERIES

Dr. Hélène Chevrou-Séverac, Ph.D.;
Head of the Health Economics function, Global; Nestlé Health Science

Post-surgical complications in gastrointestinal surgery

Despite improved surgical techniques, post-surgical complications in gastrointestinal (GI) patients remain high, as these surgical procedures can be complex. Indeed, surgical site infections (SSI) incidence after elective colorectal resection has been shown to rise up to 25% in American hospitals[15]. In Switzerland, the risk of complication in GI surgery was estimated to be 15% in well-nourished patients and 40% in malnourished ones based on the Nutrition Risk Screening (NRS) 2002 score[4]. In the UK, a recent audit done on all GI cancer centres found that the complication risk reached 19.4% following gastrectomy and 29.8% following oesophagectomy[11].

In GI cancer surgery, the main infectious complications relate to surgical site infections including wound infections, fistula, abdominal abscesses, pneumonia and urinary tract infections (UTI). In addition, the GI surgical patients are also at risk of non-infectious complications such as anastomotic leaks[16].

Immunonutrition as a strategy to reduce risk of complication in GI cancer surgery

Immunonutrition (IN), containing arginine, fatty-acids and nucleotides, has been demonstrated in many meta-analyses of randomized clinical trials to be an effective strategy to decrease post-surgical risk of infectious and non-infectious complications in various surgeries, including GI cancer surgeries[2,3,5,8,9,16].

This article presents the impact of using immunonutrition in decreasing the cost of treating complications in GI cancer surgery. Based on the meta-analysis by Waitzberg et al. (2006)[16] which estimated the relative risk of each complication's type when using IN peri-operatively, an analysis of cost impact was undertaken. Firstly, the additional cost of treating each of these complications was estimated from the HCUP 2008[7], a database representative of US hospitals, by retrieving cost of hospital stay for GI cancer surgical patients, based on their international classification disease (ICD)-10 code for diagnostic and ICD-9 code for the interventions. Secondly, a regression analysis was performed to estimate the contribution of each complication to the cost of hospital stay. Finally the relative risk from Waitzberg's study was applied to the cost of each complication to assess savings likely done by hospital for GI cancer surgical patients using IN.

Estimated cost of treating post-surgical complications in GI cancer patients

In order to estimate the cost of treating complications in GI cancer surgical patients, a regression analysis of the cost of stay of GI cancer patients undergoing surgery on the different types of post-surgical complications was performed. The cost of stay was used as the dependent variable and the type of complications as in Waitzberg[16] study as the independent variables. The complications considered in the analysis were: wound infections, fistula, abdominal abscesses, pneumonia, urinary tract infections and anastomotic leak. The regression analysis allows estimating the link between the dependent and the independent or explanatory variables. Hence from the regression analysis, each estimated coefficient linked to an explanatory variable (i.e. the complication's type) will give the contribution the complication to the cost of hospital stay. If a coefficient is close to zero, the complication does not contribute to the cost of stay. If the coefficient is positive (and significantly different from 0), its value represents the contribution of this particular complication to the cost of hospital stay. Similarly the contribution of each complication to the length of hospital stay was also estimated (see table 1). First of all, all the complications considered contributed to the cost and length of hospital stay of the GI cancer surgical patients. When looking at each complication, pneumonia and sepsis increased by more than $50,000 the cost of stay; whereas cost contribution of abdominal abscess was of $16,000 and of less than $10,000 for UTI and anastomotic leak, followed by less than $5,000 for wound infection. Similarly, pneumonia and sepsis contributed more to expending the length of hospital stay (by 14 to 15 days) than the other complications.

Table 1: Estimated cost of treating each complication's type

Patients without CC		Incremental cost or length of stay due to complication					
Estimated coefficients*		Wound infection	Abdominal abscess	Pneumonia	UTI	Sepsis	Anastomotic leak
Cost US$2010 (SE)	$19,802 (1,793)	$2,556 (2,373)	$16,995 (1,907)	$57,075 (9,805)	$8,998 (1,315)	$56,208 (4,147)	$7,607 (1,227)
LOS in days (SE)	7.05 (0.09)	1.92 (0.54)	6.16 (0.52)	14.37 (2.12)	4.61 (0.43)	15.32 (1.02)	3.90 (0.21)

Abbreviations: SE, standard error; US, United States; LOS, Length of Stay; UTI, Urinary Tract Infection.
* Estimation done by RTI Health Solution from HCUP cist database 2008, upon request from Nestlé Health Science

Impact of using immunonutrition on cost of complications

Use of immunonutrition in GI cancer patients undergoing surgery has been demonstrated in Waitzberg's meta-analysis[16] to decrease the risk of wound infection, abdominal abscess, pneumonia, UTI, sepsis and anastomotic leak. The table 2 reports the relative risk of each complication coming from this meta-analysis. Pooled percentage of patients presenting with each complication has been computed from the meta-analysis for the control and the IN groups. Finally, the cost of each complication (CC) estimated in table 1 are reported below. The cost of treating complications in the control and the IN groups have been calculated by multiplying the percentage of patients presenting with the complication to the cost of treating it. Finally, the difference in treatment cost between the two groups is computed in the last column to assess savings done by reducing complication when using IN peri-operatively.

When considering each complication, although the percentage of patients presenting with each of them was already low in the control group ranging from 3.6% to 10.5%, IN decreased significantly the percentage of patients with complications. IN was more efficient in reducing the following complications: abdominal abscess by 57% (RR=0.43), anastomotic leak by 48% (RR=0.52), pneumonia by 46% (RR=0.54) and wound infection by 39% (RR=0.61); whereas the reduction in UTI and sepsis was not statistically significant. Finally the associated reduction in treatment cost when using IN ranged on average from $95 to $2740. These values can be cumulative, depending on the number of complications faced by some patients. Thus immunonutrition is an effective and cost-savings option to reduce risk of post-surgical complications in GI cancer patients.

Conclusion

Although surgical techniques have improved, gastrointestinal cancer surgeries remain complex and can lead to complications, such as wound infection to pneumonia. Costs of treating these complications in US hospital have been estimated to range from $2,556 to $57,075 per hospital stay. Therapeutic strategies exist to improve recovery of patients and decrease risk of infectious and non-infectious complications. Among these strategies, use of immunonutrition, a specialized oral and enteral nutrition support containing arginine, omega-3 fatty acids and nucleotides, has already be proven to decrease risk of infections and complications in well- and malnourished GI cancer patients undergoing surgery[2,5,6,9,14]. Immunonutrition has also been proven to reduce hospital cost for treating these patients in the US, Germany, Italy, Switzerland and the United Kingdom [1,2,4,10,13,15]. When considering specific post-surgical complications such as wound infection, pneumonia, abdominal abscess and anastomotic leak, IN can also reduce the cost burden of treating these complications.

Table 2: Relative risk of complication and savings in reducing cost of treating complications

Outcome Variable	IN group	Control group	RR	Cost of CC	Cost of CC	Cost of CC	Difference
	N=442	N = 447	(95% CI)		Control group	IN group	
Wound infection	5.90%	9.60%	0.61* (0.38, 0.96)	$2,556	$245	$151	-$95
Abdominal abscess	2.00%	4.70%	0.43* (0.21, 0.91)	$16,995	$799	$340	-$459
Pneumonia	5.70%	10.50%	0.54* (0.34, 0.87)	$57,075	$5,993	$3,253	-$2,740
Urinary tract infection	2.50%	4.50%	0.53 (0.23, 1.19)	$8,998	$405	$225	-$180
Sepsis	1.60%	3.60%	0.53 (0.22, 1.27)	$56,208	$2,023	$1,012	-$1,012
Anastomotic leak	3.40%	6.50%	0.52* (0.28, 0.95)	$7,607	$494	$259	-$236

* means significantly different from 1 with p-value<0.05, from Waitzberg et al. (2006) 16, table 7, page 1601.

1. Braga M, Gianotti L, Vignali A, Schmid A, Nespoli L, Di Carlo V. Hospital resources consumed for surgical morbidity: effects of preoperative arginine and omega-3 fatty acid supplementation on costs. Nutrition. 2005;21(11-12):1078-1086. 2. Braga M, Gianotti L. Preoperative immunonutrition: cost-benefit analysis. JPEN J Parenter Enteral Nutr. 2005;29(1 Suppl):S57-61. 3. Cerantola Y, Hübner M, Grass F, Demartines N, Schäfer M. Immunonutrition in gastrointestinal surgery. Br J Surg. 2011;98(1):37-48. 4. Chevrou-Séverac H, Pringot C, Cerantola Y, Wasserfallen J-B, Demartines N and M. Schäfer: Cost-Effectiveness Analysis of Immunonutrition for Gastrointestinal Cancer Surgical Patients. ESICM conference 2011. Poster 2120: Intensive Care Medicine 2011: Vol 37, Suppl 1, S35. 5. Drover JW, Dhaliwal R, Weitzel L, Wischmeyer PE, Ochoa JB, Heyland DK. Perioperative use of arginine-supplemented diets: a systematic review of the evidence. J Am Coll Surg. 2011;212(3):385-399, 399.e1. 6. Grass F, Cerantola Y, Schäfer M, Müller S, Demartines N and M. Hübner. Perioperative nutrition is still a surgical orphan: results of a Swiss-Austrian survey. European J Clin Nutr (2011) 65, 642–647. 7. Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample (NIS). Agency for Healthcare Research and Quality Web site. http://www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed May 18, 2011. 8. Marik PE, Zaloga GP. Immunonutrition in high-risk surgical patients: a systematic review and analysis of the literature. JPEN J Parenter Enteral Nutr. 2010;34(4):378-386. 9. Marimuthu K, Varadhan KK, Ljungqvist O, Lobo DN. A meta-analysis of the effect of combinations of immune modulating nutrients on outcome in patients undergoing major open gastrointestinal surgery. Ann Surg 2012, 255:1060–1068. 10. Mauskopf J, Candrilli S, Chevrou-Severac H, and Ochoa J.B; "Immunonutrition for gastrointestinal cancer surgical patients: an effective and cost-savings intervention", World J Surg Oncology 2012, 10:136. 11. National Oesophago-Gastric Cancer Audit report, 2010; The NHS Information Centre. Available at: http://www.ic.nhs.uk/webfiles/Services/NCAS/Audits%20and%20reports/NHS%20IC%20OGC%20Audit%202010%20interactive.pdf. 12. Schiesser M, Müller S, Kirchhoff P, Breitenstein S, Schäfer M, Clavien PA. Assessment of a novel screening score for nutritional risk in predicting complications in gastro-intestinal surgery. Clin Nutr. 2009 Aug;27(4):565-70. 13. Senkal M, Zumtobel V, Bauer KH, et al. Outcome and cost-effectiveness of perioperative enteral immunonutrition in patients undergoing elective upper gastrointestinal tract surgery: a prospective randomized study. Arch Surg. 1999;134(12):1309-1316. 14. Smith R, et al. Wound infection after elective colorectal resection. Ann Surg 2004; 239(5): 599–605. 15. Strickland A, Brogan A, Krauss J, Martindale R, Crosse B. Is the use of specialized nutritional formulations a cost-effective strategy? A national database evaluation. JPEN J Parenter Enteral Nutr. 2005;29(1 Suppl):S81-91. 16. Waitzberg DL, Saito H, Plank LD, et al. Postsurgical infections are reduced with specialized nutrition support. World J Surg. 2006;30(8):1592-1604.

PROPER USE OF VASOPRESSORS IN SEPTIC SHOCK

Marc Leone, *MD, PhD*

Department of Anaesthesia and Reanimation and Trauma Centre Nord University Hospital Marseille, France

Benoit Ragonnet, *MD, PhD*

Department of Anaesthesia and Reanimation and Trauma Centre Nord University Hospital Marseille, France

Claude Martin, *MD, PhD*

Department of Anaesthesia and Reanimation and Trauma Centre Nord University Hospital Marseille, France

claude.martin@ap-hm.fr

Introduction

Several factors contribute to organ dysfunction in septic shock patients, and once the inflammatory response has been activated, many organ systems can be adversely affected. A marked fall in systemic vascular resistance results from arterial and venous dilatation. This is accompanied by leakage of plasma into the extravascular space, leading to relative hypovolemia. The microcirculation is adversely affected, with maldistribution of blood flow. Importantly, oxygen is neither reaching nor being effectively extracted by cells, probably because of arteriovenous shunting or abnormalities in cellular metabolism.

At the organ level, blood flow and perfusion pressure are regulated by two control mechanisms. The first, extrinsic, involves a complex interaction of vasomotor effects between opposing neurohormonal systems. The second, intrinsic, is the organ autoregulation, and depends on changes in afferent arteriolar tone in response to the organ perfusion pressure itself. In healthy subjects below the autoregulatory thresholds, organ blood flow becomes linearly dependent on perfusion pressure. In septic shock patients, the autoregulation system is disturbed resulting in this linear relation between organ blood flow and perfusion pressure. Haemodynamic factors such as volume depletion, low cardiac output or inappropriate vasodilation resulting in systemic hypotension may directly produce organ hypoperfusion through a reduction in organ perfusion pressure. Therefore, one goal of the haemodynamic resuscitation in septic shock should be restoration of adequate organ perfusion pressure without impairing blood flow to the organ.

> *"dopamine administration is associated with greater mortality and a higher incidence of arrhythmic events, making norepinephrine the first choice for the treatment of septic shock"*

Objectives in the Initial Resuscitation from Septic Shock

According to the Surviving Sepsis Campaign guidelines, the endpoints of initial resuscitation (first six hours) are: central venous pressure of 8-12 mmHg, mean arterial pressure above 65 mmHg, urine output above 0.5 ml/kg/hour, and central venous (superior vena cava) oxygen saturation ($ScvO_2$) above 70% (Dellinger et al. 2008).

Several limitations should be underlined about these guidelines on sepsis management:

- Specific endpoints remain undetermined for resuscitation in late septic shock;
- The use of central venous pressure to assess preload responsiveness is controversial because of its poor predictive value; thus, the use of dynamic parameters, as opposed to static parameters, could be preferred when predicting fluid responsiveness in septic patients; and
- The best level of mean arterial pressure is still unknown, although a target goal of 65 mmHg seems equivalent to higher pressures. Abnormalities of oxygen distribution in septic shock can subsist despite normal blood pressure. A normal or elevated $ScvO_2$ with increased lactataemia surrogates for a defect of peripheral oxygen utilisation. A prominent feature of sepsis is a dysfunction of microcirculation, with impaired perfusion and regional tissue oxygenation causing a deficit in oxygen extraction.

The Use of Vasopressors

Vasopressor agents should be used according to practical considerations in septic shock patients (Table 1). The basic catecholamine structure is a phenylethylamine with three hydroxyl groups. The effects of catecholamines range from pure α-agonist to pure β-agonist (Table 2). Briefly, the α-agonist stimulation produces a vasoconstriction, whereas the β-agonist stimulation increases cardiac performance. Pure β-agonist will not be considered thereafter.

Dopamine is the immediate precursor of norepinephrine. At low doses D1A receptors are activated causing vasodilatation of the renal and mesenteric circulations. At doses of 2-10 µg/kg/min, β-adrenergic stimulation has positive inotropic and chronotropic effects, while at higher doses, α-adrenergic stimulation results in peripheral vasoconstriction.

Norepinephrine is the endogenous mediator of the sympathetic nervous system and has both α- and β-adrenergic dose dependent effects. Large doses increase

Table 1. Use of Vasopressor Agents in Septic Shock

Criteria for prescribing a vasopressor agent
• No response to fluid infusion
• Mean arterial pressure ≤ 60 mmHg (emergently if ≤ 40 mmHg)
• Oliguria
• High lactate level
Criteria of effectiveness
• Mean arterial pressure > 60-70 mmHg
• No decrease in cardiac index or $ScvO_2$*
• Reestablishment of urine output
• Decrease in blood lactate level
• Adequate skin perfusion
• Adequate level of consciousness
Criteria for modulating the dose
• Decrease (15-20%) in cardiac index or $ScvO_2$* (< 70%) (consider using dobutamine)
• Mean blood pressure ≥ 80-90 mmHg

$ScvO_2$: central venous blood oxygen saturation

blood pressure via an α-adrenergic mediated vasoconstriction. Norepinephrine induces vasoconstriction visibly in many vascular beds (eg, the skin and muscles), and could therefore alter visceral blood flow and, more notably, renal blood flow, impairing organ function. In experimental rat models, norepinephrine caused ischemia-induced acute renal failure (Cronin et al. 1978). However, it is not clear whether the same scenario of vasopressor-induced visceral hypoperfusion actually occurs in sepsis, which is characterised by marked vasodilation related to muscle α-adrenergic receptor hyporesponsiveness or massive nitric oxide production.

Table 2. Adrenergic Receptor Effects of Catecholamines

Drug	Dose	$\alpha_{1\ art}$	$\alpha_{1\ ven}$	β_1	β_2	DA
Epinephrine	Low-dose	+	+	++++	++++	0
	High-dose	++++	++++			
Norepinephrine		+++++	+++++	+++	?	0
Dopamine	Low-dose	0	+++	+++	+++++	++++
	High-dose	++++	+++	+++++		
Dobutamine	5 µg /kg/min	+	?	++++	++	0
Isoproterenol	0.0015 µg /kg/min	0	0	+++++	+++++	

Art: arterial; ven: venous; DA: dopaminergic

When normal haemodynamic status exists, norepinephrine administered to raise mean arterial pressure by 20% does not affect glomerular filtration. In contrast, when severe vasodilation (ie. low systemic vascular resistance and high cardiac index) affects systemic circulation, the infusion of norepinephrine, which is required to restore tissue perfusion pressure, is accompanied by a restoration of urine filtration, a decrease in serum creatinine level, and an increase in clearance of creatinine in septic patients.

The beneficial effect of norepinephrine in septic patients is in agreement with the conclusions of several clinical reports. Epinephrine is synthesised, stored and released from the chromaffin cells of the adrenal medulla. At low doses, stimulation of β1- and β2-adrenergic receptors is preponderant while at higher doses (0.15-0.3 µg/kg/min), α-adrenergic receptors are activated with a potent vasoconstriction (Table 2). Epinephrine increases oxygen delivery in septic shock by increasing cardiac index without having an effect on systemic vascular resistance index or pulmonary artery occlusion pressure. It has been associated with an impaired effect at the level of splanchnic circulation. Actually, in a study by Meier-Hellmann et al., the decrease in splanchnic blood flow with epinephrine occurred in conjunction with three signs of deteriorating tissue oxygenation in this region: a decrease in splanchnic oxygen consumption, a decrease in pHi, and an increase in lactataemia.

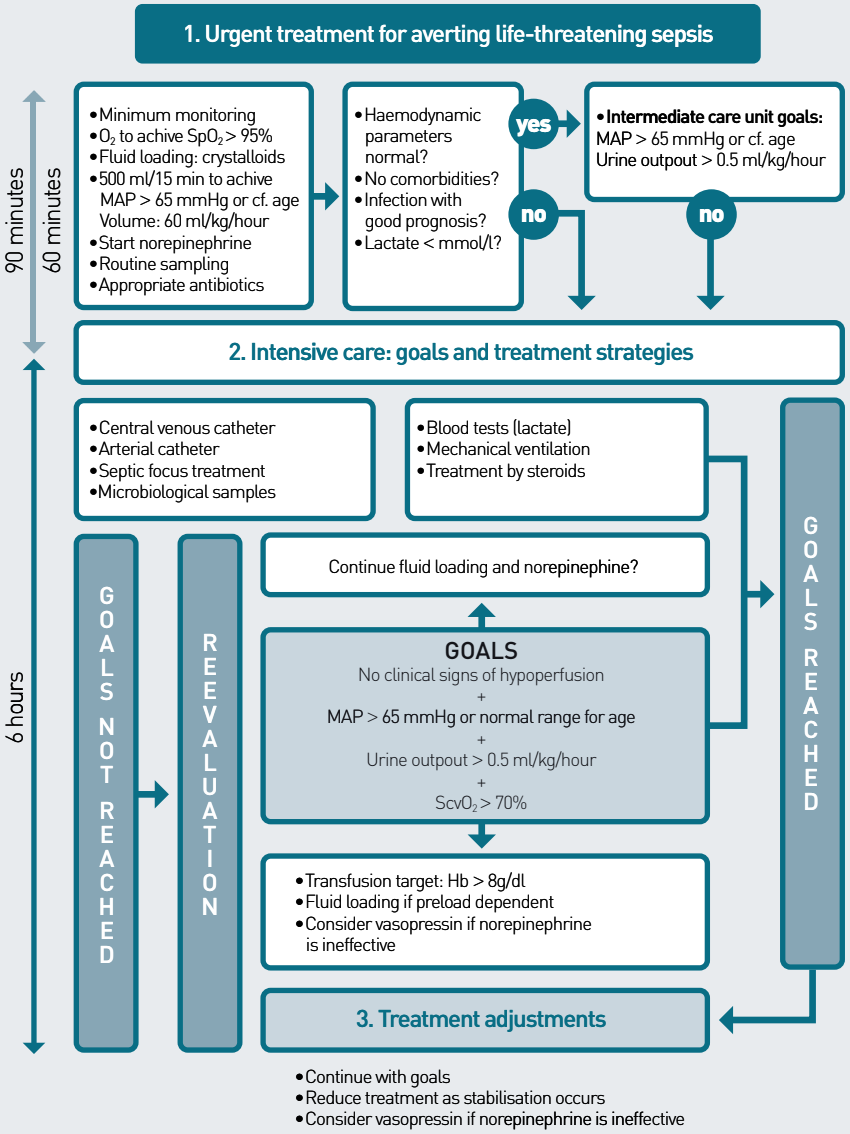
The Clinical Studies

Martin and colleagues compared the ability of dopamine and norepinephrine to reverse haemodynamic and metabolic abnormalities in human hyperdynamic septic shock. Norepinephrine was found, at the doses tested, to be more effective and reliable than dopamine in reversing the abnormalities of hyperdynamic septic shock. In the great majority of the patients, norepinephrine was able to increase mean perfusing pressure without apparent adverse effects on peripheral blood flow or on renal blood flow. At the same time, oxygen uptake was increased. In a non-randomised study, the same group found better survival in patients treated with norepinephrine than in those treated with dopamine or epinephrine (Martin et al. 2000).

Two studies seem to confirm that administration of dopamine can be associated with increased mortality in septic shock patients (Levy et al. 2005; Sakr et al. 2006). In a population of 110 septic shock patients, resistance to dopamine was associated with an increased risk of death (odds ratio: 9.5; 95% confidence interval: 3-25) (Levy et al. 2005). The dopamine group of an observational study which included 1,058 patients with shock had a higher hospital mortality rate than patients given other vasopressor agents (42.9% versus 35.7%, a statistical significance of P=0.02) (Sakr et al. 2006).

The stimulation of α-adrenoreceptors, by inducing contraction of mesenteric vascular smooth muscle, can result in gut ischemia. The effects of dopamine, norepinephrine and epinephrine on splanchnic circulation have been compared in patients

Figure 1. Summary of Haemodynamic Management of Septic Shock



with septic shock (De Backer et al. 2003). Dopamine was progressively withdrawn and replaced successively by norepinephrine and then epinephrine to maintain constant mean arterial pressure (moderate shock) or to increase mean arterial pressure above 65 mmHg (severe shock). This study showed that dopamine and norepinephrine have similar haemodynamic effects, while epinephrine can impair splanchnic circulation in severe septic shock.

Recent randomised studies showed that this splanchnic effect does not impact on patient outcome. In a French study which aimed to compare the efficacy and safety of administering norepinephrine plus dobutamine with those of epinephrine alone in 330 randomised septic shock patients, there was no significant difference between the two groups with regard to mortality rate (Annane et al. 2007). Some years later, a large randomised trial compared dopamine and norepinephrine in 1,679 patients. Among these patients, 1,044 had a septic shock (De Backer, 2010). Although there was no significant difference in deaths from the two groups, the use of dopamine was associated with a greater number of adverse events. De Backer and his team later conducted a meta-analysis in septic shock patients treated with either dopamine or norepinephrine. Six randomised studies were retrieved, totalling 2,769 patients (De Backer et al, 2012). The conclusion was clear: dopamine administration is associated with greater mortality and a higher incidence of arrhythmic events, making norepinephrine the first choice for the treatment of septic shock. The practical use of norepinephrine is summarised in Figure 1.

A Role for Vasopressine

Over time, vascular responsiveness to catecholamines diminishes. This vascular hyporeactivity to catecholamines is most likely due to excessive nitric oxide formation associated with an activation of ATP-sensitive potassium channels and a reduction in calcium entry through voltage-gated calcium channels. Thus, the search for alternative vasopressors, used alone or in combination with standard therapies, is of great interest. Vasopressin mediates vasoconstriction via V1-receptors, which are coupled to phospholipase C, and increases intracellular calcium concentration. The plasma vasopressin levels of septic shock patients are almost always increased at the initial phase of septic shock, and subsequently decreased.

A large randomised clinical trial entitled VASST study aimed to compare the survival of 778 septic shock patients treated with vasopressin (up to 0.03 IU/min) or norepinephrine (Russel et al. 2008). The inclusion criterion was septic shock requiring at least 5 µg/min of norepinephrine for six hours during the last 12 hours. Target mean arterial pressure was 65-75 mmHg. Lactatemia and renal function were unaffected by the two treatments and mortality was similar in both groups (35.4% versus 39.3%, P=0.26). The survival of patients with less severe forms of shock, defined by an entry dosage of norepinephrine ranging from 5 to 14 µg/min, was higher in the group treated with vasopressin (26.5% versus 35.7%, P=0.05). Three hypotheses may explain this result. First, the significance could be due the 5% probability of a mistake in the statistical test. Second, vasopressin may have beneficial hormonal actions, independent of its vasopressor effect. Third, the addition of vasopressin may be inefficient in the patients treated with high doses of norepinephrine. In a recent meta-analysis, the potential role of vasopressin or terlipressin was evaluated. Overall, it was concluded that these drugs do not provide any survival benefit (Polito et al. 2012); they have a sparing effect on norepinephrine requirement. They can be considered as rescue therapy when catecholamines fail to improve blood pressure.

Conclusion

Vasopressor agents are required to maintain a minimal level of blood pressure in septic shock patients. Recent evidence suggests that norepinephrine should probably be the first choice in these cases. In several studies, dopamine is associated with a poor outcome and more negative side-effects.

Vasopressin improves the norepinephrine-mediated vessel smooth muscle contraction and its use is associated with a cardiac output decrease, which can be detrimental in selected patients. However, its use does not impact on the outcome of septic shock patients. Early combination of norepinephrine and vasopressin in cases of septic shock should be tested in future studies.

Key Learning Points

1) Fluid resuscitation is always the first step in haemodynamic management.
2) The use of norepinephrine or epinephrine can be left at the discretion of the treating physician, but norepinephrine should probably be the first choice.
3) Low-dose vasopressin administration remains an option for catecholamine-refractory septic shock.
4) The potential benefit of early vasopressin use in combination with a moderate dose of norepinephrine remains to be determined.
5) The status for dopamine remains to be determined. ■

References

Albanese J et al. (2004). Renal effects of norepinephrine in septic and nonseptic patients. Chest, 126:534-539.

Annane D et al. (2007). Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomised trial. Lancet, 370:676-684.

De Backer D et al. (2010). Comparison of dopamine and norepinephrine in the treatment of shock. N Engl J Med, 362,779-789.

De Backer D et al. (2012). Dopamine versus norepinephrine in the treatment of septic shock. Crit Care Med, 40, 673-679.

Dellinger RP et al. (2008). Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Crit Care Med, 36,296-327.

Levy B et al. (2005). Cardiovascular response to dopamine and early prediction of outcome in septic shock: a prospective multiple-center study. Crit Care Med, 33:2172-2177.

Martin et al. (2000). Effect of norepinephrine on the outcome of septic shock. Crit Care Med, 28:2758-2765.

Polito A et al. (2010). Vasopressin for treatment of vasodilatory shock : an ESICM systematic review and meta-analysis. Intens Care Med, 38, 9-19.

Russel JA et al. (2008). Vasopressin versus norepinephrine infusion in patients with septic shock. N Engl J Med, 358, 877-887.

Sakr Y et al. (2006). Does dopamine administration in shock influence outcome? Results of the Sepsis Occurrence in Acutely Ill Patients. Crit Care Med, 34:589-597.

AUTHOR GUIDELINES

ICU MANAGEMENT

Content

Articles may focus on any management or practice issue in intensive care related to economics, quality of care or patient outcome. We only accept scientific papers with a clear connection to management and practise issues. We also invite opinions for publication in our Viewpoints section, which can be personal opinions of the author and/or reactions to articles published in prior issues. These are published at the discretion of the editors. Submissions may not have been published previously or be currently submitted for publication elsewhere. Articles must be written by independent authorities and any sponsors for research must be named. If manufacturers are named in an article, the text must present an unbiased view, not in support of any particular company.

Submission Guidelines

Authors are responsible for all statements made in their work, including changes made by the editor and authorised by the submitting author. The text should be provided as a word document via email to editorial@icu-management.org. Please provide a contact email address for correspondence. Following review, a revised version, which includes the editors' comments and recommendations, is returned to the author (at the contact email address) for authorisation.

Length

- Articles: maximum 1400 words (less if figures or tables are included)
- Viewpoints: maximum 700 words
- News/research/product updates: maximum 200 words

Please note that contributions longer than the specified number of words may not be accepted.

Structure

Article texts must contain:

- Title
- Names of authors with abbreviations for the highest academic degree
- Affiliation: Department and institution, city and country
- Main authors are requested to supply a portrait photo (see specifications below)
- Summary of one or two sentences (no more than 30 words) describing the content
- Contact name for correspondence and an email address which may be published with the article
- Website, if appropriate
- Acknowledgements of any connections with a company or financial sponsor
- Introduction, main text and summary/conclusion, with subheadings as appropriate
- Authors are encouraged to include checklists and/or guidelines, which summarise findings or recommendations
- References or sources, if appropriate, as specified below

Writing Style

Articles must be written in UK/British English (e.g. organisation, not organization), with short sentences, a clear structure (see above) and no bias. Full stops in numbers may only be used to indicate a decimal place; otherwise use commas as separators.

Images

Main authors are asked to supply a portrait photo for publication with their article. This and any other relevant images for publication with an article should be sent by email as separate files (only high resolution images with 300dpi) and their order of placement in the article must be clearly indicated. Only the electronic formats ".tif" or ".jpg" can be used for images, i.e. not Microsoft Word or PowerPoint. Images must be no smaller than 9cm x 9cm at 100% scale. Only images meeting these specifications can be published. If an image has been published before, permission to reproduce the material must be obtained by the author from the copyright holder and the original source acknowledged in the text, e.g. © 2012 Marianna Keen.

Format for References

Any references that are deemed important to understanding of the article should be cited in concise form within the article. Please use the Harvard reference system. Citations within the text for a single author reference should include the author surname and year of publication; for a citation with two authors include both author surnames and year of publication; for more than two authors, include the first author surname followed by "et al." and the year of publication. Multiple citations should be separated by a semicolon, and listed in alphabetical order.

Example of within text citation: (Edwards 2004; Edwards and Miller 2002; Miller et al. 2003).

Reference lists should be alphabetised by lead author and included at the conclusion of the submission.

Example of standard journal reference: Sydow Campbell, K. (1999) "Collecting information; qualitative research methods for solving workplace problems", Technical communication, 46 (4) 532-544.

Authors are responsible for the accuracy of the references they cite.

Acceptance

It is always at the discretion of our editorial board to accept or refuse submissions. We will respond to submissions within 8 weeks of receipt. We reserve the right to revise the article or request the author to edit the contents, and to publish all texts in any MindByte Communications journal, on the Internet and to list them in online literature databases.

Thank you,
The ICU Management Editorial Team
editorial@icu-management.org

VENTILATOR ASSOCIATED PNEUMONIA: BREAKING THE BRIDGE

Andrea Coppadoro, *MD*

Department of Experimental Medicine
University of Milan-Bicocca
San Gerardo Hospital
Monza, Italy

Riccardo Pinciroli, *MD*

Research Fellow
Massachusetts General Hospital
Boston, US

Lorenzo Berra, *MD*

Department of Anaesthesia and Critical Care
Massachusetts General Hospital
Boston, US

In this article we look at strategies for preventing lower airway colonisation, focusing on the factor that is widely-believed to be the main culprit forventilator associated pneumonia (VAP) development: the endotracheal tube (ETT).

VAP and its Pathogenesis

Ventilator associated pneumonia, defined as occurrence of pneumonia at least 48–72 hours after commencement of mechanical ventilation, is known to be associated with increased hospital stay and costs (Chastre 2002). However, its impact on mortality is currently under debate (Bekaert et al. 2011; Forel et al. 2012).

The main cause for VAP development is currently believed to be the ETT, rather than the ventilator. The presence of an ETT is an independent risk factor for developing VAP. The ETT disrupts the cough reflex, promotes accumulation of tracheobronchial secretions and microbial biofilm, and provides a direct conduit for pathogenic microorganisms to reach the lower respiratory tract by gravity draining through micro-channels around the cuff, and by gravity detaching from the inner lumen. The ETT acts thereby as a bridge for oropharingeal pathogens to colonise the lower airways, potentially leading to an infectious process. Several strategies to prevent VAP have been developed, targeting the role of the ETT as the main pathogenic factor involved in its development.

Preventing Biofilm Build-up

Soon after intubation, a thin layer of biofilm is present on the inner surface of the ETT. During mechanical ventilation, biofilm thickness increases because secretions tend to accumulate inside the ETT, thus reducing the volume available for airflow, despite the regular use of a suctioning catheter. Aggregates of biofilm pathogens can be detached via suctioning maneuvers or simply via mechanical ventilation; these then reach the lower airways. Data suggest that the same pathogens present in the ETT biofilm cause lower respiratory tract colonisation, leading to VAP (Gil-Perotin et al. 2012). Different strategies have been employed to reduce or remove biofilm inside the ETT by means of anti-bacterial drug coatings or cleaning devices.

Coating

The ETT can be coated with a large variety of substances; however, only two coatings have been tested in clinical trials. In a trial involving 46 ICU patients who were randomised to be intubated with either a standard or coated ETT, silver-sulfadiazine coating proved to be effective in preventing ETT bacterial colonisation (Berra et al. 2008). Furthermore, in a large randomised trial by Kollef and colleagues, involving more than 1,500 patients, the use of silver-coated ETTs reduced the incidence of microbiologically proven VAP (Kollef et al. 2008). Silver is effective because its ions penetrate inside the pathogen's membrane and interfere with nucleic acids replication, preventing proliferation.

An alternative approach to inducing biofilm pathogens' cell death is topical photosensitisation. This technique is based on a photosensitising agent (methylen blue plus photoreacting agent) and a light diffuser catheter that activates the agent, leading to formation of oxygen radicals. Though photosensitisation has been studied only in vitro, it has shown promising results in reducing bacterial survival of P. Aeruginosa and Methicillin resistant S. Aureus strains (Biel et al. 2011; Berral et al. 2008).

Another approach involves changes in material topography in an attempt to limit pathogen adhesion. Pathogens easily adhere and form biofilms on the hydrophobic polyvinylchloride (PVC) surface, a standard ETT. The chemical treatment of a PVC surface forms roughness at the nanometer level, resulting in reduced surface hydrophobicity and reduced bacterial adhesion (Loo et al. 2012). In vitro results have shown the combination of nanorough ETT and the presence of a fructose coating is effective in decreasing biofilm formation (Durmus et al. 2012). Although promising, the efficacy and safety of these techniques still need to be tested in the clinical setting.

Cleaning the ETT

The physical removal of biofilm from the inner lumen of the ETT was proposed by Kolobow and colleagues in 2005 (Kolobow et al. 2005). A dedicated device called the Mucus Shaver, consisting of an inflatable balloon with rubber rings embedded, proved to be effective in removing biofilm from ETTs used in animal models. Recently, a randomised trial showed the safety and feasibility of the

COVIDIEN
positive results for life

TAPERGUARD™ REDUCES MICROASPIRATION BY AN AVERAGE OF 90%.[1,3]

MALLINCKRODT™ TAPERGUARD™ CUFF

MALLINCKRODT™ HI-LO™ CUFF

Introducing the new Mallinckrodt™ TaperGuard™ endotracheal tubes.

Endotracheal tube cuffs are there for a reason — to prevent aspiration. The problem is, most cuffs are limited in their ability to perform this function. In fact, a recent study found that conventional cuffs *"have failed to demonstrate effective prevention of leakage in vitro and in vivo."*[1]

Now, there's a better choice. Mallinckrodt™ TaperGuard™ endotracheal tubes can reduce microaspiration an average of 90% compared with our own Mallinckrodt™ Hi-Lo™ cuffs.[3] The taper-shaped cuff helps create a better fit for your patients.[4,5]

To learn more about Mallinckrodt™ endotracheal tubes, visit us at ESICM hall A, booth #28

YOU LIVE AND BREATHE PATIENT SAFETY.
SO DO WE.

use of the Mucus Shaver in a clinical setting; bacterial growth and biofilm thickness were reduced in the ETTs of treated patients (Berra et al. 2012). While the Mucus Shaver is not commercially available, other devices with intended similar use are present on the market (Rescue Cath from Omneotech, a cleaning device from endOclear LLC, and a closed suction system from BIOVO Technologies). Whether or not physical biofilm removal is effective in VAP prevention still needs to be assessed; however, the importance of biofilm removal might also extend to other means, such as its relevance in maintaining the antibacterial properties of a coated ETT (Berra et al. 2006). Clinical studies are needed to assess whether coating and regular biofilm removal act synergistically.

Preventing Drainage from the Oropharynx

Other than via the presence of biofilm, a method in which pathogens can reach distal airways is through drainage from the hypopharynx. Standard ETTs are equipped with high-volume, low-pressure PVC cuffs, which fold against the tracheal wall forming micro-channels between the hypopharynx and the subglottic space. Maintenance of cuff internal pressure is crucial to preventing microaspirations, and continuous control through a dedicated device is effective in reducing the drainage of gastric contents into the airways (Nseir et al. 2011). Although the pressure of the ETT cuff is adequate, secretions drain towards the subglottic space. Several strategies have been proposed to prevent secretion drainage, such as subglottic secretion drainage (SSD) systems, cuff modifications to limit the presence of micro-channels and removal and anti-gravitational positioning to prevent the movement of secretions from the ETT and the hypopharynx into the lower airways.

Subglottic Drainage

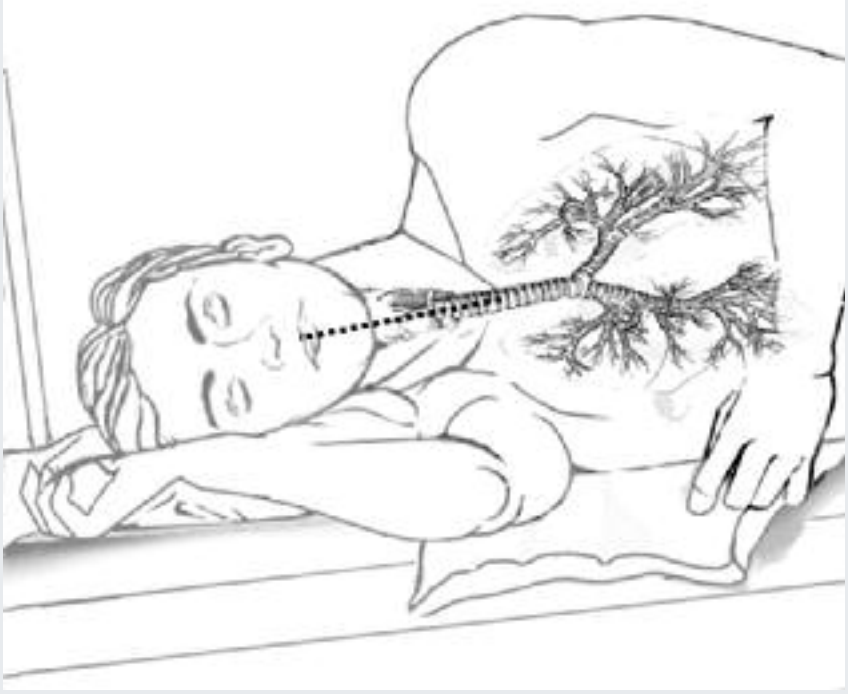
SSD systems usually consist of a small accessory lumen on the ETT, with a subglottic opening, connected to a negative-pressure generator. The material present above the ETT cuff in the subglottic space is removed, continuously or intermittently, through the accessory lumen. A randomised clinical trial on more than 300 ICU patients showed a reduction in VAP incidence in the group treated with a SSD system (Lacherade et al. 2010); furthermore, a recent meta-analysis confirmed the efficacy of SSD systems in VAP prevention (Muscedere et al. 2011).

A novel approach for subglottic drainage has been developed by BIOVO Technologies. The Airway Medix endotracheal tube is equipped with a self-expanding sleeve sealed to the tracheal mucosa, while a collecting basin built into the sleeve provides safe drainage of pooled subglottic secretions. Another strategy to removing secretions is the Mucus Slurper (Kolobow et al. 2006), which consists of a modified ETT, equipped with a series of small suctioning channels opening at the tip. An aspiration system removes through the suctioning channels both secretions leaked through the cuff and the biofilm present on the inner lumen of the ETT. No clinical data are currently available about the efficacy of the Mucus Slurper.

Cuff Material and Shape Modifications

Many materials have been proposed to substitute PVC cuffs, such as poliurethane (PU), lycra and latex, which have demonstrated better sealing in vitro. The use of materials other than PVC should reduce the formation of microchannels, resulting in reduced secretion drainage. However, in the clinical setting, only PU cuffs have been evaluated. The use of PU-cuff equipped ETTs resulted in lower postoperative pneumonia in a population of cardiac surgery patients (Poelaert et al. 2008). The combination of PU cuff and SSD was effective in reducing VAP in a clinical randomised trial (Lorente et al. 2007); however, it is not clear how much of the preventive effect is attributable to the use of a PU cuff. Another approach to limiting the folding of the cuff surface is to modify the shape of the cuff using a tapered shape rather

Figure 1. Lateral Trendelenburg Position: A vertical line from the sternal notch to the ETT connector piece, passing through the middle of the trachea should be used as a surface landmark. The patient should always be positioned to maintain this line, which is oriented slightly below horizontal.



than the classical cylindrical one. Although ETTs equipped with tapered cuffs resulted in better sealing in vitro, the clinical effect of this approach on VAP prevention still needs further investigation.

Positioning

A novel approach that has been proposed to reduce the movement of pathogens towards the distal airways is the adoption of the lateral head-down position, otherwise known as the lateral Trendelenburg position (Figure 1). This involves maintaining the main axis of the trachea slightly below the horizontal plane, so that gravity will favour drainage of secretions outside the airways. In animal models, the head-down position resulted in absence of bacterial colonisation of the airways, while those in the control group were heavily colonised (Panigada et al. 2003). Moreover, mucus flow inside the ETT was dependent on gravity, being directed towards the lungs in the standard head-up position, and towards the ventilator circuit in the head-down position (Li Bassi et al. 2008). These preclinical studies are the basis for a currently ongoing clinical trial, the Gravity-VAP Trial, which compares the lateral head-down position with the standard semirecumbent position, with the aim of disclosing a new preventive measure for VAP. This project is endorsed by the European Critical Care Research Network of the European Society of Intensive Care Medicine (ESICM).

Conclusions

A passage of pathogens through the outside or the inside of the ETT, which are under gravitational forces, has been proposed as a major offender of the lungs during mechanical ventilation. Several intriguing preventive strategies have focused on interrupting the bridge of secretions or biofilm from the oropharyngeal cavity to the lower respiratory tract. Larger clinical studies need to be performed to evaluate the benefits of such novel strategies for our patients. ■

For more information on the Gravity-VAP Trial, visit:
www.clinicaltrials.gov/ct2/show/NCT01138540;
http://compartint.net/gravityvaptrial/joomla/index.php
For references please send a request to **editorial@icu-management.org**

ON-DEMAND CHEST X-RAY ORDERING IN THE ICU: PRESCRIBING EFFICACY

Mariam Alansari, *MD, FRCSI*

Department of Adult Critical Care Medicine
King Faisal Specialist Hospital and Research Centre
Riyadh, Saudi Arabia

icu_mariam@yahoo.com

Khalid Maghrabi, *MD, FCCP, MRCP*

Department of Adult Critical Care Medicine
King Faisal Specialist Hospital and Research Centre
Riyadh, Saudi Arabia

The chest x-ray (CXR) is the main imaging tool used in the intensive care unit (ICU), though sometimes its use is deemed unnecessary. Several studies have thus focused on the possibility of lowering the number of bedside CXRs performed in the ICU. It is the opinion of the authors of this paper that unnecessary CXRs need to be eliminated and replaced by an alternative technique.

Eliminating Redundant Chest Radiology

It is common for patients in the ICU, particularly those who are mechanically ventilated, to have daily routine chest radiographs in an attempt to find relevant abnormalities that would otherwise remain undetected.

> *"A review from Ioos and colleagues (2011) supports the approach for decreasing the number of CXRs ordered in the ICU, and addresses the use of alternative techniques like ultrasonography and capnography"*

A large study by Graat and colleagues evaluated the clinical value of 2,457 routine CXRs in a combined surgical and medical ICU and found that only 5.8% of routine CXRs showed new or unexpected findings, 2.2% of which warranted a change in therapy (Graat et al. 2006). Synonymous results were recorded for both medical and surgical patients.

A randomised control study of medical ICU (MICU) patients by Krivopal and his team divided MICU patients into those who received routine CXRs and those who only received non-routine (clinically indicated) CXRs. They came across a greater percentage of radiographs with significant findings, requiring intervention, in the non-routine group (26.5%) than in the routine group (13.3%) (Krivopal et al. 2003). Significant interventions included diuresis, antibiotic administration or an invasive procedure. The non-routine group also received significantly less radiographs

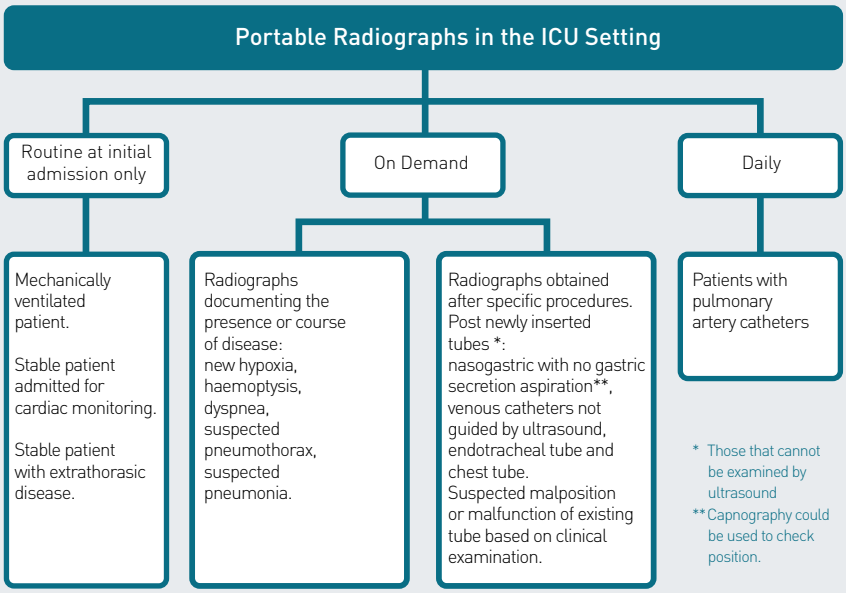


Figure 1. Indications for CXR Ordering in the ICU Setting

per person than the routine group: 4.4 versus 6.8. There was no significant difference in outcome between the groups with regard to length of intubation, ICU stay, hospital stay or mortality.

More recently, Oba and Zaza (2010) conducted a meta-analysis, for which they selected eight studies that compared on-demand approaches with daily routine strategies, including a total of 7,078 patients. No difference in ICU mortality, ICU length of stay and duration of mechanical ventilation was found between the two groups. The meta-analysis highly suggests abandoning routine CXRs.

> *"The CXR should never replace clinical evaluation of the patient but should be prescribed on the basis of clinical suspicion"*

A review from Ioos and colleagues (2011) supports the approach for decreasing the number of CXRs ordered in the ICU, and addresses the use of alternative techniques like ultrasonography and capnography in:

1. Ensuring the correct position of enteral feeding tubes when combined with epigastric auscultation;
2. Diagnosing and monitoring pneumothoraces; and
3. Post-procedural techniques after central venous catheter insertions.

Based on our review of the best currently available evidence, and on the latest recommendations following the consensus opinion of the American College of Radiology expert panel, which was revised in 2006, we can summarise the acceptable indications for ordering CXRs in the ICU (Figure 1).

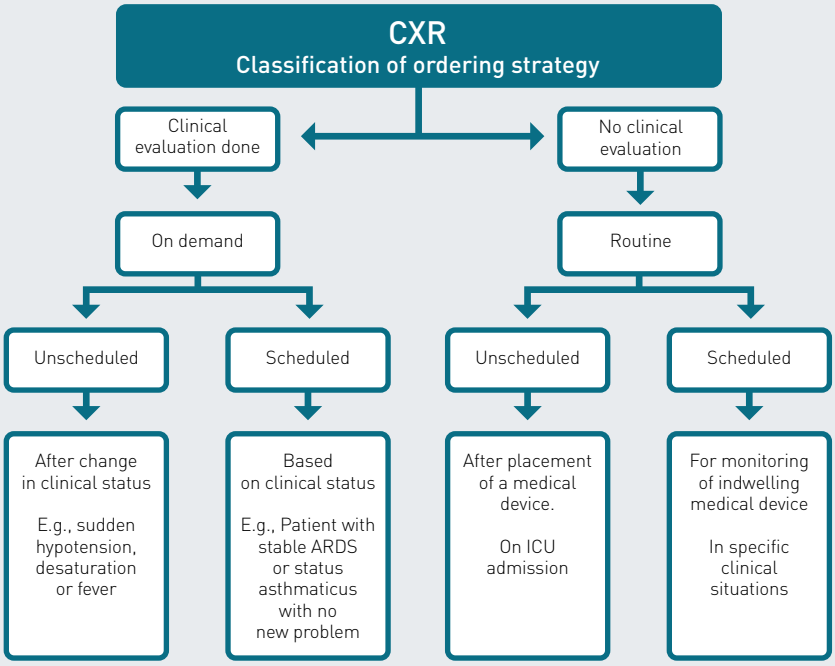


Figure 2. Suggested Classification of CXR Ordering in the ICU for Future Studies

Conclusion

Previous studies advocating daily routine chest radiography in ICUs were all observational without providing a comparison. The efficacy of daily routine chest radiography was probably overestimated in these because of inadequate study design. To help in designing future studies, it is worth mentioning that clear identification of patient population, enrollment criteria, and various definitions of efficacy (unexpected findings, new findings and findings that lead to treatment change) are needed.

The CXR should never replace clinical evaluation of the patient but should be prescribed on the basis of clinical suspicion. As a consequence, the organisation of the ICU might have to be modified to allow the implementation of such a strategy for prescription and the reduction of the number of CXRs ordered.

Future Studies

More studies are needed to help in defining a guideline for selecting the most efficient and appropriate CXR strategy. The author of this article agrees with the suggestion from Hejblum et al. (2008) that bedside CXRs in adult ICUs be categorised into four groups (Figure 2). This classification system could help in future studies to identify specific ICU situations in which unnecessary CXRs can be reduced. ■

References

Graat ME et al. (2006). Chest radiography practice in critically ill patients: a postal survey in the Netherlands. BMC Med Imaging; 6:8.

Hejblum G et al. (2008). A Web-Based Delphi Study on the Indications of Chest Radiographs for Patients in ICUs. Chest; 133; 1107-1112

Ioos et al. (2011). An integrated approach for prescribing fewer chest x-rays in the ICU. Annals of Intensive Care 1:4. Open access journal

Krivopal M et al. (2003). Utility of daily routine portable chest radiographs in mechanically ventilated patients in the medical ICU. Chest; 123(5):1607-1614.

Oba Yand Zaza T (2010). Abandoning daily routine chest radiography in the intensive care unit: meta-analysis. Radiology, 255:386-395.

DEVELOPING AND HARMONISING A PRIME SPECIALITY: INTENSIVE CARE MEDICINE

AN INTERVIEW WITH **ANDREW RHODES**

President of the European Society of Intensive Care Medicine (ESICM), Andrew Rhodes, has committed much of his time to progressing intensive care medicine as well as introducing and strengthening strategies for raising and harmonising standards in medical practice. In this interview with Managing Editor Marianna Keen, he shares some of his most recent achievements, and others he plans for the future, with a hope of changing the sector for the better on a global scale.

What do you see as your role as ESICM President and what do you hope to achieve?

In my position, I have a number of primary roles that include:

- Being the "face" of the society and ensuring that the organisation's priorities are in line with what our members would want;
- Leading the team to ensure that the business and management side of affairs runs smoothly;
- Ensuring that the activities of the society are consistent with what the society stands for;
- Expanding the society membership base;
- Actively supporting and encouraging research and education in critical care; and
- Challenging politicians to recognise intensive care medicine as a speciality.

I do, of course, have my own objectives in mind for the society. When I stood for election I described my aims as being: to increase the membership benefits available from the society; to secure the future of the society by investing in a "home" for the society; to develop a foundation that raises funds for education and research; to develop a number of innovative educational tools; and to upgrade the website and content.

In many respects we have delivered on these aims. To start with, the membership benefits of the society have significantly improved. We have made the society's e-learning system free for all members to use, re-designed the e-newsletters that are used for communication, and significantly increased the content available to members within our website. In addition, we have purchased and moved into our own office in Brussels, providing the society with a strong base from which to achieve all its future aims.

My aspiration to develop a foundation has been achieved with the launch of the LIFE-Priority fund, which is raising the profile of intensive care medicine among the general public as well as raising funds for the society's activities. Responding to my desire to develop innovative educational tools, we have invested in the Basic Assessment and Support in Intensive Care (BASIC) and Advanced Training Courses in Intensive Care (ATCIC) educational courses, and developed a systematic review unit. Finally, we are in the process of replacing our website; the re-launch should go live in October, during the ESICM congress in Lisbon.

Intensive care training courses have been the latest addition to ESICM's portfolio of educational activities. Do you believe that these courses are so far achieving their objectives?

Delivering quality education of a consistent standard to a large number of people is a significant challenge, especially delivering it to parts of the world that have few resources. We have therefore decided to support the BASIC course that originates from the University of Hong Kong. This course is effectively free to users and therefore enables us to help many countries that could not afford more expensive alternatives. We do not see our role as being able to educate the whole of Europe, rather to provide the training in each country to support the development of the country's own faculty, which can then continue to roll out the education programme themselves without our help.

In addition, we have started to develop ATCIC, which provides advanced courses that can be utilised in a similar fashion. These courses aim to be stand-alone modules with all the manuals and course materials already provided and quality checked. This is a major undertaking as these courses are extremely time consuming and intensive to develop. We now have a portfolio of five ATCIC courses: Mechanical Ventilation (beyond BASIC), Critical Care Nephrology, ICU Management, Haemodynamic Monitoring and Management, and Bronchoscopy. We aim soon to deliver many more.

What is the next step towards harmonisation of the highest level of training in healthcare, medical practice and medical specialities within the EU and the rest of the world?

This is a complex issue. Each country has evolved intensive care medicine in a different fashion and changing this is difficult and politically very sensitive. It is almost impossible to force change from the centre of Europe, so we have started a process of discussing the issue with many individual countries, at a local level, with the hope of encouraging the change. To date, Spain, Switzerland and the UK have designated intensive care medicine as a primary specialty, but many other countries are now progressing down similar routes. We have recently participated in a major

healthcare policy debate at the European Commission to discuss this issue (amongst others). It is only by engaging with all of the stakeholders that we can hope to elicit change.

Sepsis and septic shock are hot topics for discussion at present. Do you have any recent developments to share?

The management of septic shock remains very important. The European Society (together with the Society of Critical Care Medicine) initiated the Surviving Sepsis Campaign in 2002 by issuing the Barcelona Declaration that aimed to decrease the mortality from septic shock by 25%. Ten years later, the campaign has published results from its database demonstrating that the mortality has reduced by this amount, at least in part due to the increased awareness of the condition leading through to improved practice.

We have just completed the latest update for the Surviving Sepsis Campaign guidelines, which will hopefully be published in the next few months. Together with these guidelines will be an update of the sepsis bundles and a re-invigoration of the campaign, in a move to continue improving practice and outcomes.

What research projects are you currently conducting?

There are four areas that I am currently focusing my research: health services research for intensive care provision and surgical outcomes; haemodynamic monitoring; early goal directed therapy; and biomarkers for outcome.

Can you tell us more about your research on early goal directed therapy?

We have had a long interest at my institution in the use of EGDT for high-risk surgery patients. We have performed a series of studies aiming to describe this patient cohort and to explore different ways of improving the care they receive in order to improve their outcomes. Largely, this has been successful in the small single-centre setting. Further larger studies are now ongoing in order to confirm some of these findings. ■

DOES INTERMEDIATE CARE IMPROVE PATIENT OUTCOMES AND REDUCE COSTS?

Jean-Louis Vincent, *MD, PhD*

Head Department of Intensive Care
Erasme Hospital
Free University of Brussels
Brussels, Belgium

jlvincen@ulb.ac.be

In an era of rapidly progressing intensive care medicine, along with rising demand and growing concern on the bottom line, hospital managers are increasingly introducing intermediate care facilities in a move to solve the problem of overcrowded ICUs in an efficient manner; but controversy exists on whether these units really provide all the answers.

Introduction

Intensive care medicine has developed rapidly over the past 60 years or so, making the intensive care unit (ICU) an essential component of all modern hospitals and one of the most costly hospital departments. High nurse:patient ratios and a frequent need for invasive monitoring and life-support equipment make operating costs high, and as ICUs get busier and demands for the very latest tests, equipment and interventions increase, managers are faced with ever more difficult decisions regarding how best to distribute the increasingly limited finances for healthcare without reducing standards of care and negatively influencing patient outcomes.

One approach that has been proposed to reduce ICU costs and improve efficiency is the creation of intermediate care units, also called high-dependency or step-up/down units. Some hospitals may have both a high-dependency unit as an immediate step down from intensive care and then a separate intermediate care unit. For the sake of this article, however, we will use these terms interchangeably unless specified.

Intermediate care units are used for patients who need more care than a general ward can provide but do not really need the expertise or equipment, or both, of an intensive care unit. General intermediate care units have been adopted by some hospitals, while others have created intermediate care units for specific patient groups, such as cardiac, neurosurgical, or respiratory patients. But do these units really provide the intended benefits?

> *"Combining intermediate care with intensive care in one unit may actually represent a more efficient solution than having separate units"*

Can Intermediate Care Units Improve Outcomes?

Perhaps the key argument in favour of the intermediate care unit is related to the fact that many patients who are admitted to the ICU do not really need full intensive care. The presence of an alternative facility for such patients could liberate ICU beds for those patients who would benefit most from ICU access at a time when many ICUs around the world are faced with bed shortages and demand has never been greater. Indeed, 20-30% of all general ICU admissions are considered of low severity and are admitted largely for routine surveillance or monitoring for less than 24 hours; this percentage may be considerably higher on surgical ICUs than on medical or mixed units. These low severity patients generally have good outcomes and are unlikely to require any intensivist input during their ICU stay, making them good candidates for admission to an intermediate care unit rather than to an ICU, without any negative consequences on the course of their recovery being incurred. The provision of this alternative site could result in improved outcomes across the service by enabling more of the most severely critically ill patients to benefit from appropriate ICU access instead of having to be managed on general wards with inadequate equipment and staff who are not specifically trained to care for the critically ill.

Patients across the spectrum could benefit from these alternative sites. In addition to providing intermediate care to directly admitted low-risk patients requiring short-term intensive monitoring, these units are used as a step-down facility for patients who no longer need intensive

therapy, but are perhaps not ready to return to the general ward. Without the presence of an intermediate care unit, such patients would, perhaps unnecessarily, be kept on the ICU, thus occupying a bed and preventing its use by a patient who may benefit more from it.

An intermediate care unit may also limit the risks of premature ICU discharge to the ward: the change in degree of monitoring from an ICU to an intermediate facility will be smaller than if the patient is discharged straight to a general ward. Via this transition, any residual problems will theoretically be detected and managed appropriately in a timely manner. However, a potential downfall is that availability of an intermediate care facility may give a false sense of security and actually result in more premature discharges, putting patients at risk of needing readmission to the ICU, which has been associated with worse outcomes.

> "Reducing unnecessary admissions must remain a priority to ensure adequate availability of ICU beds for all those who need them, and to improve the cost-effectiveness and efficiency of our ICUs"

Can Intermediate Care Units Reduce Costs?

Intermediate care units have higher staff:patient ratios and more specialised equipment, notably for monitoring, than on the general ward but less than on the ICU. Theoretically, this makes these units a more cost-effective option for certain patients, for example, patients needing routine postoperative surveillance who are at low risk of developing complications and hence unlikely to require invasive therapy during an ICU stay. However, such patients are generally low-risk and account for a relatively low proportion of total ICU costs, so the impact on overall costs is likely to be relatively limited. Moreover, as intermediate care is more costly than general ward care, and as some patients would be managed on the general ward if no intermediate care unit were available, total hospital costs may in fact increase with introduction of such a facility. In addition, although intermediate care units have lower staff:patient ratios and possibly less invasive monitoring equipment, potentially making them less expensive to run than the ICU, overall department expenses may be increased as certain equipment will need to be duplicated on the intermediate care unit and on the ICU if these are in separate parts of the hospital. Also, staff costs may increase as both units will need to have a full allocation of personnel.

> "Twenty to thirty percent of all general ICU admissions are considered of low severity and are admitted largely for routine surveillance or monitoring for less than 24 hours"

Is There an Alternative Solution?

General intermediate care units have been introduced in many hospitals, particularly in Europe, but there is actually very little evidence that they improve patient outcomes or reduce costs. Indeed, rather than solving the problem of overcrowded ICUs and helping reduce costs, creation of intermediate care units may simply act to shift the dilemma to another site. Combining intermediate care with intensive care in one unit may actually represent a more efficient solution than having separate units for several reasons. Firstly, expensive monitoring and interventional equipment is concentrated in one area rather than needing to be duplicated. In addition, a larger combined unit provides increased flexibility of bed use and staffing than do separate units. A large unit can adapt more easily to a sudden increase in demand for beds and to changes in the types of patients admitted, such that beds and nursing staff can be used flexibly for patients with varying acuities of illness. The nursing and medical staff can also benefit from the heterogeneous nature of the patients, which make working conditions more varied and interesting. Mortality rates in larger, high volume ICUs may also be lower than in smaller units with fewer annual admission rates.

Clearly the optimal approach will vary according to local demand and available facilities, but intermediate care units should not be opened for the sole aim of improving efficiency and reducing costs, because there is little evidence that this is achieved. Rather, the way in which the available ICU beds are used should be carefully evaluated and optimised. Introduction of an intermediate care unit cannot replace the need for strict admission and discharge criteria to ensure that only patients who can truly benefit are admitted to the ICU. Many patients with no reasonable chance of survival, who will not benefit from intensive care, are still admitted to ICUs. Reducing these and other unnecessary admissions must remain a priority to ensure adequate availability of ICU beds for all those who need them, and to improve the cost-effectiveness and efficiency of our ICUs. ■

THE PORTUGUESE HEALTHCARE SYSTEM: UNIVERSAL AND COMPREHENSIVE

Paulo Alexandre Boto
Assistant to the Secretary of State
Assistant to the Minister for Health
Portugal

Fernando Leal da Costa
Secretary of State
Assistant to the Minister for Health
Portugal

Located in the south-west of Europe, with a mainland area of 91,900 km², along with the archipelagos of Açores and Madeira, Portugal is a developed country with a lot to offer, including a health system with many strengths. Amid the economic crisis and an ageing population, however, the country is facing problems in this sector. In response to this, the Ministry of Health has proposed a sustainability plan for hospitals to overcome the crisis, which anticipates improved efficiency, disease prevention and safety, among other benefits.

Overview

The total population in Portugal has seen a five percent increase over the last decade. While in the 1970s only 38.8% of the population lived in urban areas, this rose to 58.2% by 2006. Most of the population is concentrated in two large metropolitan areas: Greater Lisbon (with approximately two million inhabitants) and Greater Oporto (with approximately 1.2 million inhabitants). The number of births has been declining steadily since the 1970s and the average age has been gradually rising. In terms of production and income, total gross domestic product (GDP) in 2010 was 272.4 billion US dollars, according to current purchasing power parity (PPP) (Table 2).

In terms of health status, beyond the crude death rate in 2009 (Table 1), life expectancy at birth was 79.5 years (76.5 years for males, 82.6 years for females), which places the country just above the average, according to the Organisation for Economic Cooperation and Development (OECD). Over the past five decades, both sexes have seen similar improvements, with women currently living on average six years longer. In the past four decades, Portugal has also had one of the largest reductions in infant mortality rates among OECD member countries.

Table 1. Demographic indicators (all data from 2009, except where indicated).

Population, total (000s)	10.633
Population, female (% of total)	51,6
Population, ages 0-14 (% of total)	15,2
Population, ages 15-64 (% of total)	67
Population, ages 65 and above (% of total)	17,8
Age dependency ratio(dependants to working-age population)	0,49
Birthrate, crucle (per 1000 people)	9,4
Deathrate. crucle (per 1000 people)	9,8
Population growth (annual %)	0,1
Fertility rate, total (births per woman)	1,32
Population density (people per km2)*	113,9
Urban population (% total)**	58,2
Education level - 9 years of school (%)***	86,5

Source: adapted from Barros P, Machado S, Simoes J. Portugal: Health system review Health Systems in Transition, 2011, 13(4): 1-156
*2008, **2006, ***2007

The Organisation of the Healthcare System

The Portuguese healthcare system is a national health system (NHS) that was founded in 1979. It was formed mostly based on structures already in place (hospitals and primary care centres), but these were not necessarily organised as an integrated set of providers.

In the last few years, reforms have seen both primary care centres and hospitals grouped both horizontally and vertically, forming local health units, in order to improve management, efficiency and quality.

As is typical in Beveridge influenced systems, the Portuguese NHS and therefore its hospitals have been financed mostly with funds from general taxation. Healthcare costs have grown consistently above both the inflation rate and the increase in GDP.

Primary care and secondary care are supposed to work together in articulation. However, as is often the case, transition of both patients and information between the two levels is not as smooth as desired,

raising issues in terms of coordination and continuity of care. More recently, a third level, long-term care, has been added to the equation. Long-term care is expected to reduce the need for longer hospital stays, but the number of available beds is still insufficient.

Financing

Total health spending accounted for 10.1% of GDP In 2008, according to the latest figures from the OECD Better Life Index. This placed Portugal, in 2009, above the OECD average of 9.5%. Portugal has also typically received a slightly higher percentage of private financing than other OECD countries. This amounted to 2,508 US dollars per capita after adjusting for PPP.

Comparing total health expenditure per capita with other countries' GDP per capita, there seems to be a positive correlation between the two. Portugal is well within this trend.

Table 2. Gross Domestic Product in Portugal 2003—2010

	Unit	2003	2004	2005	2006	2007	2008	2009	2010
Gross domestic product (GDP)	Bin USD curr. PPPs	202,5	207,9	224,6	242,1	256,8	265,1	266,4	272,4
GDP per capita	USD current PPPs	19.392	19.796	21.294	22.870	24.206	24.957	25.055	25.609

Source: OECD Factbook statistics (doi: 10.1787/csp-prt-table-2011-1-en).

Table 3. Total Expenditure on Health as a Percentage of GDP

Total expenditure on health, % gross domestic product	1970	1980	1990	2000	2001	2002	2003	2004	2005	2006	2007	2008
Portugal	2,4	5,1	5,7	9,3	9,3	9,3	9,8	10,1	10,4	10,1	10,0	10,1

Source: OECD Health Data 2011 (http://stats.oecd.org/Index.aspx?DataSetCode=SHA)

Table 4. Total Number of Hospital Beds per 1,000 Population

Total hospital beds, Per 1000 population	1985	1990	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Portugal	4	4	3,8	3,7	3,6	3,7	3,6	3,5	3,5	3,4	3,4	3,3

Source: OECD Health Data 2011 (http://stats.oecd.org/Index.aspx?DataSetCode=HEALTH_REAC)

Human Resources

Portugal currently has 3.8 physicians per 1,000 population. This data refers to all physicians who are licensed to practice and thus includes doctors not actually practicing, however. In any case, this result places Portugal above the OECD average. This has been the result of a steady increase over the last five decades. In 2009, Portugal had 5.6 nurses per 1,000 population, which places it below the OECD average, in spite of considerable growth in the past decade, including significant improvements in the country's ability to train these professionals. We are thus slightly above the OECD average in the first case (albeit with a ratio of graduates to physicians below ideal), and the opposite is true when looking at nurses.

In terms of healthcare management, Portugal has had a postgraduate course in hospital management for over 40 years now. Taught by the National School of Public Health (http://www.ensp.unl.pt/), it was for a number of years a requirement to enter hospital management; recent changes to the legislation made this optional rather than compulsory. Simultaneously, other schools started teaching health services management, mostly at the postgraduate level.

The Portuguese Hospital System

Most hospitals and hospital beds in Portugal are public. Numbers of both, however, have been decreasing in recent years. The number of hospitals has decreased mostly through mergers, with several hospitals forming hospital centres, under a common executive board. The number of beds has decreased mostly as part of an international trend, associated with more effective and efficient treatments and the move of a number of activities (namely surgical) to ambulatory care. In 2009, there were 2.8 acute care hospital beds per 1,000 population.

A look at the number of acute care beds suggests these were less affected than other healthcare beds. The occupancy rate of curative (acute) care beds has for the past decade been stable around 72 %, with several experts arguing for the need to reduce the number of beds as a way to increase this rate. The average length of stay in 2009 was recorded to be 5.9 days. This too has dropped significantly over past decades.

Current Concerns

As is common elsewhere in the developed, western world, Portugal faces problems brought by an ageing population, with increased incidence and prevalence of chronic conditions and multi-morbidity. The Ministry of Health is thus currently insisting on health promotion and disease prevention as a means to ensure the overall sustainability of the system.

Eight areas of clinical and health promotion have been identified as priorities: diabetes, HIV infection and AIDS, tobacco consumption, healthy eating, mental health,

oncology, respiratory diseases, and cardio and cerebrovascular diseases.

The current government is keen on promoting actions on lifestyle changes, with a special focus on diet and exercise, while reducing the consumption of tobacco, alcohol and illicit drugs. Some of these require intersectoral policies. Target populations include the young and the elderly, with healthy and active ageing as an objective. In organisational terms, governance relies both on the national level, for policy and budgeting, and also on five regional health administrations.

Patient access to the system is still a problem in some areas, with the prevalence of long waiting lists and waiting times, particularly for elective surgery, outpatient visits and diagnostic tests. The past few years, however, have seen the development of a number of specific programmes in an attempt to overcome this situation.

In recent years Portugal has also shown particular interest in the quality of healthcare provided. There is a national strategy for quality in healthcare, which was approved in 2009, and the country has participated in global safety programmes led by the World Health Organisation (WHO), among other schemes. The Ministry of Health is also currently in the process of transposing to the Portuguese legislation the directive on cross-border care. As a part of this process, the ministry is working on the definition of referral centres to integrate with European reference networks.

All actions taken by the government follow a national health plan, stretching from 2012 to 2016. The previous plan (2004-2010) was very positively reviewed by the WHO (http://www.euro.who.int/__data/assets/pdf_file/0003/83991/E93701.pdf). Internally, comprehensive reviews are being undertaken in primary care, emergency services and long-term care, based on the advice of national experts.

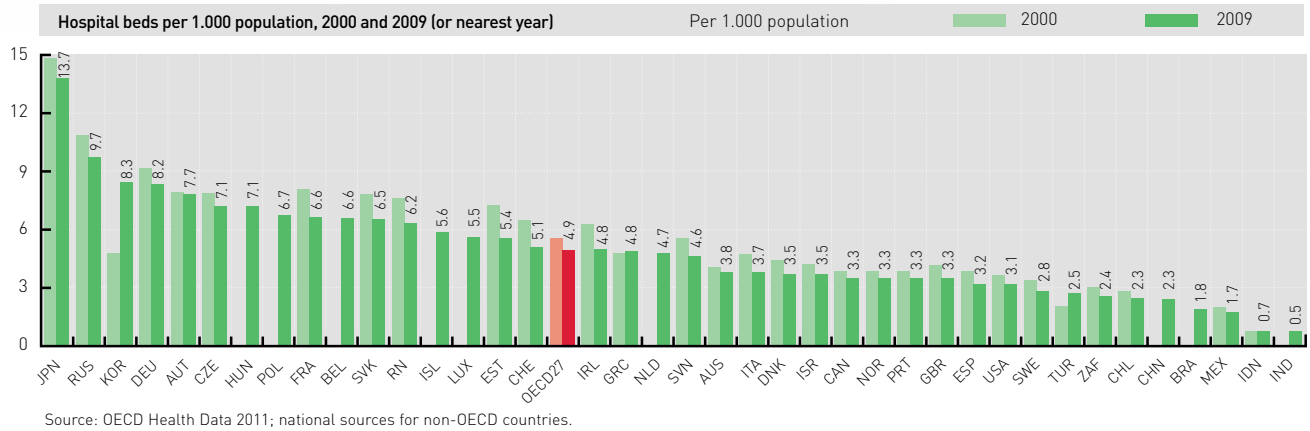
The main current issues with the Portuguese national health system are related to the current economic crisis in the country (and Europe in general), and the need to ensure the system's sustainability. In the context of the global economic crisis, the country and the healthcare system are currently under pressure to be more efficient while ensuring access and quality. The healthcare sector is thus undergoing some reform, with specific efforts directed at hospitals. These focus around eight axes:

1. **Implementing a more coherent hospital network**
   Specific measures include the redefinition of the network of hospitals, given the recent formation of several hospital centres, which group hospitals, and the existence of a number of referral networks (specialty-based) that need coherence and updating.
2. **Defining a more sustainable financing policy**
   Specific measures include the development of costing systems and the improvement of benchmarking efforts between hospitals.
3. **Integrating care to improve access**
   Specific measures include the improvement of referral criteria between primary care centres, hospitals and long-term care departments.
4. **Making hospitals more efficient**
   Specific measures include the implementation and monitoring of clinical guidelines, and raising ambulatory surgery rates.
5. **Ensuring quality as a major trait of hospital reform**
   Specific measures include a reduction of current rates of hospital acquired infections and rates of cesarean sections.
6. **Investing in information systems as a sustainability factor**
   Specific measures include the implementation of the electronic health record and guaranteeing the validity of all information in the system.
7. **Improving Governance**
   Specific measures include celebrating management contracts with the boards and assessing board performance.
8. **Strengthening the role of citizens**
   Specific measures include making hospital benchmarking public and raising patient awareness of healthcare costs.

The Ministry of Health believes this strategy to be the only way to make the Portuguese healthcare system sustainable in the face of one of the biggest economic crises seen in recent years, while at the same time improving its effectiveness, efficiency, safety, fairness, timeliness and patient-centered charactersitics. ■

For references, please send a request to **editorial@icu-management.org**

Figure 1. Hospital Beds Per 1,000 Population



Source: OECD Health Data 2011; national sources for non-OECD countries.

INTENSIVE CARE MEDICINE IN PORTUGAL: RESPONDING TO CHANGES

Luís Coelho, *MD*

Medical-Surgical Intensive Care Unit
North Lisbon Hospital Centre
CEDOC, Faculty of Medical Sciences
New University of Lisbon
Lisbon, Portugal

luismiguelcoelho16@gmail.com

João Gouveia, *MD, PhD*

Medical-Surgical Intensive Care Unit
North Lisbon Hospital Centre

gouveia.jl@gmail.com

The economic crisis in Portugal has forced the Government to impose major budget cuts in the National Health Service, and although the level of care for critically ill patients until now has remained adequate, intensive care medicine in the country is feeling limitations.

Overview

Since the first intensive care unit (ICU) to be established in Portugal was opened in Coimbra in the sixties, intensive care medicine has become a speciality of growing importance in the treatment of patients admitted to hospital, providing fundamental support to critically ill sepsis sufferers, patients admitted to the emergency room, and those admitted for a major operation or transplant surgery. The next critical care units to be introduced were in Lisbon and Oporto, predominantly in major teaching hospitals, and in the following decades ICUs were created in almost every Portuguese hospital.

In 2001, thirty years after the creation of the first ICU, there were 413 intensive care beds in 50 polyvalent ICUs (Direcção Geral Saúde, 2001). At the present time (September, 2012), there are 52 polyvalent ICUs and two ECMO centres in Portugal, providing a total of 451 intensive care beds (1.75% of all acute care beds). Unfortunately, ICU resources are not equally distributed throughout the country; most of the beds are in hospitals on the country's coastline, with the highest concentration of resources in main urban areas such as Lisbon and Oporto, and the lowest in Azores.

Despite the increase in intensive care beds seen in the last decade, compared with other countries in Europe, Portugal still has the lowest ratio of beds per 100,000 inhabitants, standing at 4.2:100,000. Due to this low ratio, the number of ICU admissions per 100,000 inhabitants is low, while patients that are admitted are of high severity. As a consequence, in 2011, the mean simplified acute physiology score (SAPS II) in the ICUs that entered data to the HELICS database was 43.4. This implies high resource use, with patients staying in the ICU for a mean length of 10.5 days, and 63.4% of patients being mechanically ventilated (3.1% non invasively) in the first three days of intensive care. ICU case mix is dominated by medical patients (58.1%) and about 80% of all patients are infected on admission.

> *"The curriculum, defined by the National Board of Intensive Care Medicine, part of the Portuguese Medical Association, is based on the Competency-Based Training programme in Intensive Care Medicine for Europe (CoBaTrICE)"*

ICU Staffing

In Portugal, as in other countries, there has been a growing shortage of intensivists, despite efforts in training new specialists. Since the economic downfall, governmental budget constraints have been reflected primarily in the recruitment of new specialists, for renewal of ICUs teams. There are currently 202 intensivists in Portugal, a number that is not sufficient to ensure 24-hour coverage in all ICU's. This has led to hospital managers recruiting non-specialised physicians to guarantee coverage. Only 59% of ICU doctors are intensive care certified, and the highest percentage of these work in northern Portugal.

Not only is there an insufficient supply of staff, but the workforce is also becoming old, with a mean age of 49.41 +/-7.39 years. This means that even using all its impending capacity, Portugal will be facing a shortage of intensivists, unless things change. With this stark reality in mind, measures are currently being taken to increase the capacity of ICUs in the main Portuguese hospitals.

Training in Intensive Care Medicine

Nowadays, intensive care medicine is a two-year subspeciality. Entry into an intensive care medicine training programme is possible following successful completion of a primary speciality, namely anesthesia, internal medi-

cine, pulmonology, cardiology or general surgery. The curriculum, defined by the National Board of Intensive Care Medicine, part of the Portuguese Medical Association, is based on the Competency-Based Training programme in Intensive Care Medicine for Europe (CoBaTrICE)—a programme from the European Society of Intensive Care Medicine (ESICM), which has extended towards harmonising intensive care medicine worldwide.

Trainees are strongly encouraged to take the European Diploma in Intensive Care Medicine (EDIC) before taking the Portuguese final approval in intensive medicine exam (Ordem dos Médicos, 2006).

Over the years, SPCI has strived to make intensive care medicine a primary speciality with five-year training and multidisciplinary pathways in a competency-based programme. The society and the Portuguese Medical Association are working together for this to become a reality in the near future.

Educational Activities

The Portuguese Society for Intensive Care promotes training and professional development, and executes several courses, such as Fundamental Critical Care Support (FCCS), Fundamental Disaster Management (FDM) and ESICM's Advanced Training Courses in Intensive Care (ATCIC) module on bronchoscopy. During a regular year, SPCI organises two to three courses that are integrated into national conferences. Students on these courses are not only undertaking medical training in intensive care, but also in other specialities, so that they may integrate critical care medicine into their primary speciality. This training is critical for physicians who regularly work in the emergency room.

Currently, SPCI organises two of the main intensive care meetings in Portugal: the National Congress, usually held in May, and a joint meeting with another Portuguese medical society, this year with the Portuguese Society of Pulmonology. Pulmão e Doente Crítico will be held in Oporto from 7–8 November. Other important meetings include Infection and Sepsis in Oporto, the Critically Ill meeting held in Lisbon in January, the Spring Meeting, and the Artificial Ventilation Update meeting (JAVA), which both take place in Oporto.

These meetings have been very important in helping physicians to recognise critically ill patients on their admission to the emergency department, so that they can be treated promptly. They also played a part in raising awareness of the Surviving Sepsis Campaign guidelines, prompting their adoption in Portuguese hospitals, as well as in educating physicians on how septic patients can be recognised early after admission. Finally, they prompted hospital managers to implement sepsis bundles outside of ICUs.

The Portuguese Society for Intensive Care has a strong relationship with the Brazilian Intensive Care Society (AMIB). Besides joint meetings between them, they share the same official journal: Brazilian Journal of Intensive Care. Soon, they will begin joint prospective studies, involving a large number of Portuguese and Brazilian ICU's. SPCI is also involved in promoting education and training in African countries where Portuguese is spoken, organising courses on disaster management and preparedness, trauma, and care of the critically ill.

The joint work of SPCI, the Portuguese Medical Association and Portuguese intensivists has been fundamental in defining intensive care medicine as a fundamental speciality in hospital care. ■

> *"SPCI is also involved in promoting education and training in African countries where Portuguese is spoken, organising courses on disaster management and preparedness, trauma, and care of the critically ill"*

References

Direcção Geral de Saúde (2001). Cuidados Intensivos. Recomendações para o seu desenvolvimento. (www.dgs.pt/upload/membro.id/ficheiros/i006185.pdf).

Ordem dos Médicos (2006). Documento orientador da formação em Medicina Intensiva. (www.ordemdosmedicos.pt).

European Society of Anaesthesiology

ESA

Barcelona, Spain

Euroanaesthesia 2013

The European Anaesthesiology Congress

June 1- 4

Symposia
Refresher Courses
Workshops
Industrial Symposia & Exhibition
Abstract Presentations

CME Accreditation
EACCME - UEMS

Deadline abstracts:
December 15th 2012
Online submission:
www.euroanaesthesia.org

ESA Secretariat
Phone +32 (0)2 743 32 90
Fax +32 (0)2 743 32 98
E-mail: registration@euroanaesthesia.org

AGENDA

NOVEMBER

6-8 10th Doppler-Echocardiography in Intensive Care Medicine
Brussels, Belgium
www.intensive.org

7-9 Sepsis 2012
Paris, France
www.sepsisforum.org

9-10 ESA Autumn Meeting
Prague, Czech Republic
www.euroanaesthesia.org

17 2nd International Fluid Academy Day
Antwerp, Belgium
www.fluid-academy.org

DECEMBER

4-6 18th Postgraduate Refresher Course on "Cardiovascular and Respiratory Physiology Applied to Intensive Care Medicine"
Brussels, Belgium
www.intensive.org

16-19 Update on Nutritional Support
Rome, Italy
www.intensive.org

JANUARY 2013

19-23 SCCM 2013
San Juan, Puerto Rico
www.sccm.org

FEBRUARY

7-8 18th International Symposium on Infections in the Critically Ill Patients
Sevilla, Spain
www.infections-online.es

MARCH

14-15 IT @ Networking Awards 2013
Brussels, Belgium
www.itandnetworking.org

19-22 33rd International Symposium on Intensive Care and Emergency Medicine (ISICEM)
Brussels, Belgium
www.intensive.org

In our Next Issue

COVER STORY
The Global ICU

MATRIX
McLaren F1 System to Monitor Health
Candida Infections

COUNTRY FOCUS
Hungary

INTERVIEW
Edgar Jimenez

Letters to the Editor & Requests for References Cited in ICU Management: editorial@icu-management.org

ICU MANAGEMENT IS PUBLISHED BY
MindBYTE Communications Ltd
9, Vassili Michailidi CY-3026 Limassol, Cyprus
E-mail: office@icu-management.org
Website: www.icu-management.org

PUBLISHER
MindByte Communications Ltd office@icu-management.org

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

SUBSCRIPTION RATES

One year	Europe	53 Euros
	Overseas	68 Euros
Two years	Europe	89 Euros
	Overseas	105 Euros

Note: Participants of the International Symposium on Intensive Care and Emergency Medicine receive a one year subscription as part of their symposium fee.

ART DIRECTOR
Tassos Kostis art1@mindbyte.eu

PRODUCTION AND PRINTING
Total circulation print and online: 12,640
ISSN = 1377-7564

REFERENCES
References cited in this journal are provided to ICU Management by the authors and are available on request at editorial@icu-management.org.

VERIFIED CIRCULATION
according to the standards of International Business Press Audits.

ICU Management is independently audited on behalf of ISICEM by AKC

REWARDING EXCELLENCE & INNOVATION

GLOBAL HEALTHCARE IT AND MEDICAL TECHNOLOGY COMPETITION

WINNING PROJECT
GETS PRIZES
WORTH € 20,000

14 - 15
MARCH 2013
Clinique St-Jean
BRUSSELS

FOR MORE INFORMATION:
www.itandnetworking.org

ITa NETWORKING AWARDS 2013