ICU

MANAGEMENT & PRACTICE

INTENSIVE CARE - EMERGENCY MEDICINE - ANAESTHESIOLOGY

VOLUME 19 - ISSUE 2 - SUMMER 2019

Paediatrics

Quality improvement in the PICU – a primer for intensivists, *N. Mehta*

PICU Up! A multicomponent early mobility intervention for critically ill children, *S. Kudchadkar*

PICU-acquired complications: the new marker of the quality of care, *K. Choong*

Caring for children in the PICU - from novel technology to family-centred care: new challenges for old needs, *E. Esteban, I. Jordan, F. José Cambra*

Virtual reality experience in the PICU, *M. Malakooti*

PLUS

Seven steps to design, procure, implement and maintain a Clinical Information System for your intensive care unit, *T. Kyprianou*

Respiratory physiotherapy in critically ill patients, *V. Comellini, S.Nava, A. Artigas*

A structural approach for diagnosing weaning failure - a case from a specialised weaning centre, *T. Frenzel, L. Roesthuis, J. van der Hoeven*

Vitamin D deficiency in ICU patients, *G. Martucci, K. Amrein, J. Ney*

Noise in the intensive care unit: where does it come from and what can you do about it? *J. Darbyshire*

Keeping the Person in Personalised Medicine, *M. Abrams*

European guidelines on the management of traumatic induced bleeding, *R. Rossaint*

Can Goal-Directed Therapy solve the economic burden of postsurgical complications? *W. Habenbacher*

05

9 771377 756005

How to improve Patient safety in the OR anaesthesia work area?

Symposium on Monday, June 3rd 2019

12:15 – 13:45 in Strauss 1 Room

Chairman: **Prof. Xavier CAPDEVILA** *(Montpellier, France)*

Medication errors in the OR: causes and epidemiology
Dr. Sven STAENDER
(Männedorf, Switzerland)

Medication safety: insights from an expert pharmacist
Dr. Edith DUFAY
(Lunéville, France)

Medication errors: how to prevent?
Prof. Joyce WAHR
(Minneapolis, USA)

EUCIS-DIPR-0319-0316

Aspen Pharma Trading Limited
3010 Lake Drive, Citywest,
Dublin 24, Ireland
aspenmedinfo@professionalinformation.co.uk
www.aspenpharma.eu

aspen

Successful **patient experience** begins here

PAEDIATRICS

It is never easy when children are in the hospital. And it is even more stressful when they're in the Paediatric Intensive Care Unit (PICU). When a child is admitted to the PICU, it means that they require the highest level of medical care. Children in the PICU present with different symptoms and conditions - from serious infections to heart conditions; from asthma to diabetes; from a traumatic injury to a drowning accident. In other words, children in the PICU are acutely ill and require highly-skilled, minute-to-minute care, and attention.

Our cover story Paediatrics discusses the treatment and management of the critically ill child. Managing a child in the PICU requires specific and consistent care and continuous monitoring. Many times, there is a need to use treatment modalities that are not available in other parts of the hospital. And these modalities often involve the use of ventilators and certain medicines (sedatives and opioids) that can only be given while keeping the child under close supervision.

Our contributors talk about these challenges and discuss clinical practices that can improve care. Nilesh Mehta talks about quality improvement tools that can help transform the paediatric intensive care unit into a highly reliable and safe environment that nurtures continuous learning and delivery of high-quality care.

Sapna Kudchadkar presents an overview of the 'PICU Up!' mobility programme at Johns Hopkins University School of Medicine, which integrates sleep promotion, delirium prevention, and sedation optimisation to increase mobilisation in critically ill children.

Karen Choong discusses PICU-acquired complications and the fact that they continue to be under-recognised amongst PICU clinicians. She highlights the importance of early recognition and the introduction of ICU based rehabilitation strategies to improve patient outcomes.

Elisabeth Esteban, Iolnda Jordan, and Francisco José Cambra discuss the challenges and opportunities to improve care and practice in the PICU and talk about the family-centred model and how it is essential to provide the best care for children.

Marcelo Malakooti talks about the use of virtual reality and how critically ill children at all developmental levels can benefit from interactive experiences that provide positive stimulation that otherwise are absent from the ICU environment.

In our Informatics and Technology section, Dr. Theodorus Kyprianou outlines seven steps to design, procure, implement and maintain a Clinical Information System for the intensive care unit and how such a system needs to be adapted and customised to fit local healthcare professionals' and patients' needs.

In our Matrix section, Vittoria Comellini, Stefano Nava, and Antonio Artigas talk about respiratory physiotherapy in critically ill patients and how it represents a fundamental part of the standard practice in ICU. They provide an overview of the physiotherapeutic tools and strategies that can be applied to critically ill patients. Tim Frenzel, Lisanne Roesthuis and Johannes G van der Hoeven talk about a structural approach for diagnosing weaning failure and highlight the importance of prescribing an individualised treatment plan. Gennaro Martucci, Karin Amrein, and Julia Ney provide a review on the role of vitamin D in critically ill patients and the potential benefit of vitamin D supplementation.

In our Management section, Julie Darbyshire presents practical measures and interventions to reduce noise levels in the ICU and to improve the patient experience. She highlights the importance of a wider understanding of the types of noise that can be most disturbing and the consequences of constant disturbance on patients. Mark P. Abrams highlights the importance of Person in Personalised Medicine and why it is crucial to maintain a focus on the patient-doctor relationship in order to more fully optimise patient care.

Our interview section features Rolf Rossaint, Professor of Anaesthesiology, RWTH University Aachen, Germany. Prof. Rossaint has published several high-quality studies dealing with the treatment of severe acute respiratory distress syndrome (ARDS) and has also been actively involved in research on the pathophysiology of trauma associated coagulopathy and possible treatments. He discusses these new guidelines with ICU Management & Practice.

Managing the critically ill child is no small feat, especially when we are in the midst of a paradigm shift from a culture of sedation and immobility to a culture of mobilisation and early recovery. PICU teams need to work together to implement this change and to provide high-quality care using advanced treatment strategies that are safe and effective for children. ■

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

Jean-Louis Vincent

Jean-Louis Vincent
Editor-in-Chief
ICU Management & Practice

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

JLVincent@icu-management.org

@ICU_Management

IN EVERY ISSUE

COVER STORY

Point of View

INFORMATICS AND TECHNOLOGY

MATRIX

MANAGEMENT

INTERVIEW

Venue

Point of Care ultrasound

Simple. Fast. Precise.

Venue™ is a powerful ultrasound system which helps simplify your patients' care.

Empowering you with:

- Simple user interface
- Fast advanced automation tools
- Precise visualization

Venue tools and automation help you focus on what's most important – your patient.

For more information or to arrange a demonstration, please contact your GE sales representative or visit gehealthcare.com/venue

gehealthcare.com

Use of sedation and controlled paralysis in ICU patients with ARDS

According to a National Institutes of Health sponsored clinical trial that was conducted at several North American hospitals and was led by clinician-scientists at the University of Pittsburgh and University of Colorado schools of medicine, reversibly paralysing and sedating hospitalised patients with severe breathing problems does not prove improve patient outcomes in a large majority of cases. Findings were presented at the American Thoracic Society's Annual Meeting and are published in the New England Journal of Medicine.

This trial was conducted to settle an ongoing debate within the critical care medicine community as to whether it is better to paralyse and sedate patients in acute respiratory distress or to avoid heavy sedation to improve the patient's recovery. According to senior author Derek Angus, Chair of PITT's Department of Critical Care Medicine, this issue has always been a dilemma for clinicians since many well-done clinical studies show that temporarily paralysing patients to improve mechanical breathing could save lives. But it is not possible to paralyse a patient without heavy sedation. As per the findings of the trial, sedation results in worse recovery, hence providing the answer to this long-standing debate that sedation with intermittent short-term paralysis is as good as deep sedation with continuous paralysis.

The trial - Re-evaluation Of Systemic Early neuromuscular blockade (ROSE) is the first of the National Heart, Lung, and Blood Institute's (NHLBI) Prevention & Early Treatment of Acute Lung Injury (PETAL) Network. The network conducts clinical trials designed to prevent diseases or treat patients who are at risk for acute lung injury or acute respiratory distress syndrome (ARDS). One of the key areas of emphasis for the PETAL Network is early detection, and that is why every member institute of this network is required to include critical care, emergency medicine, acute care or trauma principal investigators. This is to ensure that critical issues are recognised and triaged, and the odds of patient recovery are improved before they even get to the intensive care unit.

> **"sedation with intermittent short-term paralysis is as good as deep sedation with continuous paralysis"**

The ROSE trial has already enrolled 1006 patients in 48 US and Canadian hospitals. The patients were enrolled within hours after the onset of moderate to severe ARDS. Half of the patient population was given a 48-hour continuous neuromuscular blockade and heavy sedation while the other half was given light sedation. Study clinicians had the option of giving a small dose of neuromuscular blockade that would wear off within an hour to ease respiratory intubation.

James Kiley, Director of the Division of Lung Diseases at the NHLBI, explains that the PETAL network wants to conduct trials that would help answer these important questions. The results of these trials can help clinicians make decisions early on so that they can provide better care for patients with ARDS.

The idea for the ROSE trial originated because of findings from another trial in 2010 that reported reduced mortality with neuromuscular blockade. All participants in that French trial were heavy sedated, whether they received the neuromuscular blockade or not. But in North America, clinicians have been trying to stay away from heavy sedation as it is associated with cardiovascular complications, delirium, and increased difficulty weaning patients from mechanical ventilation.

Findings from the ROSE trial show that patients who received the neuromuscular blockade and were highly sedated developed more cardiovascular issues while in the hospital. However, no significant difference was found in mortality between the two groups at three months, six months, or 12 months follow-up.

The study has completed enrolment ahead of schedule, and it is believed that findings will soon be available for healthcare providers, which could result in rapid implementation of enhanced care for ARDS patients. Derek Angus has said that so far, the results suggest that avoiding paralysis and deep sedation is the best practice for most patients who are hospitalised for breathing problems. But future trials will have to test whether there is a subpopulation of patients with ARDS who could still benefit from neuromuscular blockade. ■

Reference

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome. The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network. New England Journal of Medicine.

New recommendations for stroke systems of care - American Stroke Association policy statement

Approximately 7.2 million Americans 20 years or older have had a stroke. Nearly 800,000 people in the U.S. have a new or recurrent stroke each year. A stroke occurs every 40 seconds in the U.S., and someone dies of a stroke every four minutes.

According to a policy statement published by the American Stroke Association, and published in the journal Stroke, improvements in stroke systems of care are imperative to ensure advancement in the treatment and care of stroke patients and to improve patient outcomes. The statement was released during the National Emergency Medical Services (EMS) Week. Over the last decade, stroke systems have seen vast improvements in the availability of endovascular therapy, neurocritical care, and stroke centre certification. The use of telestroke and mobile stroke units have further improved access for stroke patients to alteplase, a lifesaving, clot-busting drug.

As Opeolu Adeoye, the chair of the writing group for the statement and associate professor of emergency medicine and neurosurgery at the University of Cincinnati points out, there have been monumental advancements in acute stroke care over the last 14 years. The concept of a comprehensive stroke system of care has evolved. This new policy statement reflects the progress that has been made so far and highlights what still needs to be done to maximise patient outcomes.

As per the statement, if more than one intravenous alteplase-capable hospital is within reach, EMS should consider additional travel time of up to 15 minutes to reach a hospital that is capable of performing endovascular thrombectomy for patients who have had a severe stroke. Both these treatments, intravenous alteplase, and endovascular thrombectomy, should be administered as soon as possible to be effective. However, not every hospital can deliver these services. As Adeoye points out, getting to the hospital quickly is important for patients with a large vessel blockade, but so is getting to the right hospital.

The new policy statement from the American Stroke Association also addresses disparities in care among racial and ethnical minorities, who are less likely to use EMS and who also have the lowest awareness of the causes and symptoms of stroke.

> "getting to the hospital quickly is important for patients, but so is getting to the right hospital"

This lack of knowledge, especially among the Hispanic and black population, can hamper timely stroke care. That is why the American Stroke Association has emphasised on the importance of implementing public education programmes that focus on stroke systems and highlights the importance of seeking emergency care by calling 9-1-1 if stroke symptoms are observed.

Other recommendations include:

- Implementation of local and regional public education initiatives to increase awareness of symptoms with an emphasis on high-risk populations.
- The need for EMS leaders, governmental agencies, medical authorities, and local experts to work together and to adopt consistent and standardised triage protocols to rapidly identify patients with a known or suspected stroke.
- For certified stroke centres to provide help to stroke survivors to reduce the risk of subsequent strokes, as per the guidelines for secondary prevention.
- To design a stroke system that provides comprehensive post-stroke care, including primary care and specialised stroke services including physical, occupational, speech, and/or other therapies needed at time of discharge.
- To enact policies to standardise the organisation of stroke care, to lower barriers to seeking emergency care for stroke, to ensure that stroke patients receive care at the right hospital at the right time, and to facilitate access to secondary prevention of rehabilitation and recovery resources after stroke.

Overall, the goal of these recommendations is to create optimised stroke systems of care. The American Heart Association's Get With The Guidelines - Stroke at U.S. Hospitals have been associated with an 8% reduction in mortality at one year and improved functional outcome at the time of discharge.

Reference

Adeoye, O et al. (2019) Recommendations for the establishment of stroke systems of care: a 2019 update: a policy statement from the American Stroke Association. Stroke.

Cocoon bed aims to lower ICU delirium

The intensive care unit environment can be extremely stressful, even if they provide some of the best care in the world. It is believed that a patient in the ICU has their sleep interrupted approximately every three minutes either through noise, lights, or medical intervention. Up to 80% of patients in the ICU suffer from some form of delirium, and nearly 30% develop post-traumatic stress disorder.

In order to improve the treatment of patients in the ICU and to lower the rates of delirium, Brisbane's Prince Charles Hospital Foundation has designed the world's first hospital bed that is being called the "Intensive Care Cocoon." The cocoon features noise-cancelling technology that removes the incessant beeping of monitoring equipment from the patient's head. It also stimulates day and night, and allows patients to view a live video of their home so that they can talk to their family members and their pets.

As Prof. John Fraser, the director of the Critical Care Research Group at Prince Charles Hospital in Brisbane points out, a stay in the ICU can seem like the worst jet-lag ever, and while patients with critical conditions are treated in the ICU, there are environmental factors that often worsen mortality, increase time in hospital and overall frighten people. He highlights the fact that the risk of mortality at six months increases by 300% in patients with delirium.

Patients have been known to suffer from anxiety during their ICU stay and from PTSD after. For some, the ICU can be the scariest place they've ever seen. It is thus evident that there is a need to address this issue and to focus on improving the patient experience in the ICU.

The Prince Charles Hospital Foundation plans to build two prototypes of the beds if it is able to raise $1 million in donation. These beds might be expensive to build, but if rolled out across hospitals, it is believed that they can make intensive care cheaper in the long run and can reduce the length of time patients stay in the ICU.

Reference

The Common Good. People Powering Medical Discoveries. An initiative of the Prince Charles Hospital Foundation.

Big Data and subtypes of sepsis

Results of a study conducted by the University of Pittsburgh School of Medicine suggests that sepsis is not one condition, but many conditions that could benefit from different treatments. The findings are published in JAMA and were presented at the American Thoracic Society's Annual Meeting.

Sepsis is the number one killer of hospitalised patients and is a life-threatening condition that arises when the body's response to infection begins to injure its own tissues and organs. It has been over a decade, and no major breakthroughs have happened in the treatment of sepsis. The only improvement observed so far is the enforcement of the "one-size-fits-all" approach for prompt treatment, highlights Christopher Seymour, associate professor in Pitt's Department of Critical Care Medicine and member of Pitt's Clinical Research Investigation and Systems Modeling of Acute Illness Center. But as he explains, these protocols ignore the fact that all sepsis patients are not the same. It is a condition that kills nearly 6 million people annually, and using a one-size-fits-all approach is unacceptable for such a huge threat to patients.

By seeing sepsis as several different conditions, and with varying clinical characteristics, it may be possible to discover and test therapies that are tailored to treat the different subtypes of sepsis.

The "Sepsis ENdotyping in Emergency Care" (SENECA) project, funded by the National Institutes of Health (NIH), has used computer algorithms to analyse 29 clinical variables found in the electronic health records of more than 20,000 patients who had sepsis within six hours of hospital arrival. Patients were clustered into four distinct sepsis types, which include:

1. Alpha - found to be the most common (33%) and with the least organ dysfunction and lowest in-hospital death rate at 2%.
2. Beta - found in approximately 27% of patients; mostly elderly patients with the most chronic illness and kidney dysfunction.
3. Gamma - almost the same frequency as beta; but associated with greater inflammation and pulmonary dysfunction.
4. Delta - least common at around 13%; most deadly type, often associated with liver dysfunction and shock; showed highest in-hospital death rate at 32%.

After studying another 43,000 sepsis patients, the UPMC team confirmed these findings. These findings were then applied to recently completed international clinical trials that tested different therapies for sepsis. None of these trials had anything significant to report. However, results might have been different if the trial participants had been classified on the basis of these four subtypes. For example, early goal-directed therapy (EGDT) was not found to have any benefit following a five-year study, but when the UPMC team re-examined the results, they found that it could have benefitted the Alpha type of sepsis patients but would result in worse outcomes for the Delta subtype.

If you think about it logically, the theory of sepsis subtypes makes perfect sense. Just like all breast cancer patients do not receive the same treatment (as some breast cancers can be more invasive and require aggressive treatment), the same is true for sepsis. There is thus a need to find therapies that apply to specific types of sepsis and then design clinical trials to test those therapies.

Reference

Seymour CW et al. (2019) Derivation, Validation, and Potential Treatment Implications of Novel Clinical Phenotypes for Sepsis. JAMA.

Sedation with dexmedetomidine in critically ill patients

Dexmedetomidine is used to sedate patients while maintaining a certain degree of sustainability. The use of dexmedetomidine is known to reduce the duration of mechanical ventilation and delirium among patients in the intensive care unit (ICU). However, its use as the sole sedative agent in patients undergoing mechanical ventilation has not been studied extensively.

An open-label, randomised trial was conducted with 4000 critically ill adults who had been undergoing ventilation for less than 12 hours in the ICU. These patients were expected to receive ventilator support for longer than the next calendar day. Patients either received dexmedetomidine as the sole sedative or usual care with propofol, midazolam, or other sedatives. The primary outcome of the trial was the rate of death from any cause at 90 days and the target range of sedation-scores on the Richmond Agitation and Sedation Scale was -2 to +1 (lightly sedated to restless).

As per the results of the trial, the primary outcome event occurred in 566 of 1948 patients in the dexmedetomidine group, and in 569 of 1956 patients in the usual-care group. In order to achieve the required level of sedation, patients in the dexmedetomidine group received supplemental propofol, midazolam, or both during the first two days after randomisation, while the same drugs were administered as primary sedatives in the usual-care group. It was observed that the incidence of bradycardia and hypotension was more common in the dexmedetomidine group.

> **"patients undergoing mechanical ventilation in the ICU and who received dexmedetomidine for sedation had a similar rate of death at 90 days compared to the usual-care group"**

Findings from this trial suggest that patients undergoing mechanical ventilation in the ICU and who received dexmedetomidine for sedation had a similar rate of death at 90 days compared to the usual-care group. The dexmedetomidine group needed supplemental sedatives to achieve the required level of sedation. Overall, the dexmedetomidine group reported more adverse events compared to the usual-care group.

Reference

Shehabi Y et al. (2019) Early Sedation with Dexmedetomidine in Critically Ill Patients. New England Journal of Medicine.

Use of opioids in the ICU not linked to continued prescriptions

According to a new study, opioids prescribed in the intensive care unit (ICU) do not drive risks for continued use or prescriptions. The findings were presented at the American Thoracic Society (ATS) 2019 International Meeting in Dallas, TX.

Opiate abuse is a major healthcare issue. In the U.S., opioid-related deaths have increased more than three-fold from 2000 to 2016. The use of opioids in the ICU have to follow guidelines that are adjusted to a standard based on necessary opiate exposure only. This applies to parenteral opioids and oral opioids.

The study was conducted with 3102 opiate-naive patients admitted from 2016-2017. 45% of these patients received opioids in the ICU and were exposed according to their prescription. As a general profile, opioid-receiving patients were younger, with greater weight, height, APACHE scores, and greater lengths of stay in both the hospital and the ICU. The primary outcome of the study was opioid prescriptions within 1-year post-discharge.

Study investigators from the Cleveland Clinic and Duke University Medical Center shared the findings that patients who were prescribed opioids in the ICU did not report an increase in the risk of continued opioid prescription at 1 year after discharge. These findings thus support the guideline set by the Society of Critical Care Medicine regarding the management of pain, agitation, and delirium.

Healthcare providers should continue to address pain optimally and should manage patients in the ICU by using the comprehensive bundle to provide comfort as well as prevent delirium.

Reference

Chen A et al. (2019) Use of Opioids in the Medical Intensive Care Unit Is Not Associated with Outpatient Opiate Use. ATS International Conference. Available from abstractsonline.com/pp8/#!/5789/presentation/26085

Nilesh M. Mehta
Associate Professor of Anesthesia
Harvard Medical School

Director of Quality & Outcomes
Critical Care Medicine
Boston Children's Hospital,
Boston, USA

President, American Society for Parenteral & Enteral Nutrition (ASPEN)

nilesh.mehta@childrens.harvard.edu

@NileshMehtaMD

Quality improvement in the PICU – a primer for intensivists

Quality improvement provides tools that help the transformation of an intensive care unit into a highly reliable and safe environment, that nurtures continuous learning and delivery of high-quality care that improves patient experience and outcomes.

Despite advances in healthcare and dramatic improvements in survival across the spectrum of disease states, there exists a chasm between ideal care and actual healthcare delivery globally (NASEM 2018). In the U.S., consistent high-quality health care remains elusive in the increasingly complex and subspecialised healthcare system (IOM 2001). Quality improvement (QI) has emerged as a strategy to address the defects in the healthcare system, to achieve the best care that improves patient experience and outcomes. We will discuss some of the concepts of the QI process, with particular emphasis on the paediatric intensive care unit (PICU) environment.

Definition

High-quality care is consistent with evidence base and professional knowledge, and it is characterised by an increased likelihood of achieving desired outcomes (IOM 2001). The IOM report outlined six dimensions of quality in healthcare: i) safety (avoiding patient harm), ii) effectiveness (avoiding overuse and underuse), iii) patient-centredness (focused on patient needs), iv) timeliness (avoiding harmful delays), v) efficiency (avoiding waste, affordability to system), and vi) equity (IOM 2001; NASEM 2008). Avedis Donabedian described a model with three main areas for assessment of quality; structure, process, and outcome – the SPO framework – this model guides the practical application of QI concepts. The patient perspective is central to this framework, and QI efforts must be focused on the patient experience and outcomes during illness.

Challenges to quality improvement in the PICU

The PICU environment is characterised by complexity of care, therapeutic choices, time sensitivity for interventions, constantly changing workflow, competing priorities and a complicated interaction between the provider, patient and the healthcare environment (**Figure 1**). Large amounts of visual real-time data that need to be interpreted in the context of changing patient status and the interface with devices, create opportunities for unpredictable errors and harm. Healthcare-associated infections, medication errors, device-related safety issues, and failure to provide timely therapies are some of the events seen in this environment. Human behavioural factors, such as knowledge gap, fixation, alarm fatigue and failure to effectively communicate and collaborate are often deemed as causal factors for errors. In addition, lack of engagement from the frontline providers, disruption of autonomy and competing priorities in the unit result in a perception of QI efforts as a burden, time constraint and top-down mandates that are not deemed worthwhile. Lack of leadership buy-in can be a major factor in the failure to sustain QI efforts in the PICU. The PICU environment (structure, devices, workflow) and its interaction with providers is a critical factor in preventable harm, with faulty systems design often the root cause. A highly reliable ICU must incorporate a thoughtful and intelligent design and structure that facilitates the delivery of high-quality care.

> **PICU leaders must embrace a culture of safety, continuous improvement and ensure a safer environment for patients and providers**

High-reliability organisations/systems

In order to successfully mobilise change and ensure high-quality care delivery, the PICU must embrace the culture of high reliability (Hines AHRQ 2008). Highly reliable organisations (HRO) are characterised by extended periods without catastrophic accidents or serious failures, despite operating in a highly complex and hazardous domain. A highly reliable PICU nurtures a culture of continuous quality improvement, has strong, engaged and motivating leaders who cultivate resilience in the system by prioritising safety over other performance demands. The five characteristics of an HRO are: i) preoccupation with failure; ii) reluctance to simplify explanations for operations, successes, and failures; iii) sensitivity to operations (situational awareness); iv) deference to frontline expertise, and v) commitment to resilience.

Smart PICU design

Preferably conceived at its inception, a strategic PICU design creates an environment (workspace and workflow) that is suitable for

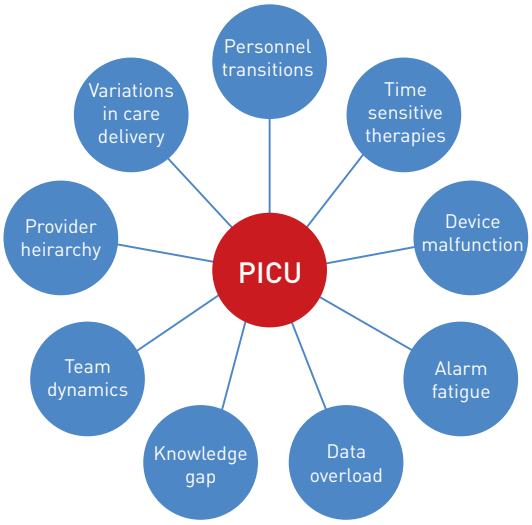


Figure 1. Challenges in the PICU environment that may impede its transformation into a high reliability system.

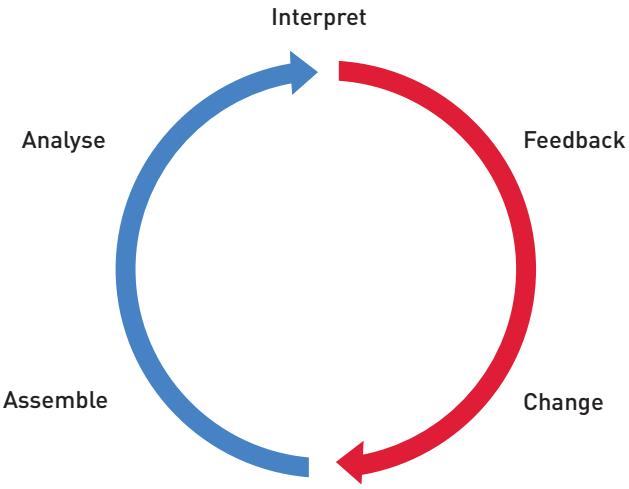


Figure 2. The Learning Healthcare System Cycle (Friedman 2014)

safe and effective care provision by committed providers, while also optimising patient and provider experiences. Patient rooms are designed to promote infection control procedures, early mobility, and patient comfort. A smart ICU room may also monitor and track changes in light, noise and other environmental hazards. Intelligent summarisation of data, smart alarm management, and patient privacy are other key aspects of the ICU design (Halpern 2014).

Optimising PICU workflow

Thoughtfully developed and standardised key processes such as patient rounds, handoffs during admission, transfers and discharges, medication reconciliation and safety huddles have become an integral part of daily workflow in the PICU. The use of a checklist or a more robust decision support tool that integrates patient data in real time facilitates some of these processes during rounds in many PICUs. Protected space for undisturbed performance of high-risk tasks, such as medication check, structured assessment tools for sedation and pain, tracking the evolution of illness severity using early warning scores are examples of nursing QI and safety processes aimed at improving patient safety in the PICU. In a highly reliable PICU, providers continue to explore the environment for potential disasters, are willing to speak up for safety, and strive for prevention or early detection and mitigation of harm.

Culture of continuous QI and Learning healthcare systems

A highly reliable PICU invests in data gathering. Patient level data are analysed in the context of existing knowledge base to develop best practices using the concepts of implementation science, an important tool that completes the cycle of a Learning healthcare system, depicted in **Figure 2**. The commitment to learn from every event or data stream is at the core of this cycle. The lessons learnt from this interpretation and past experience, are immediately made available for clinical decision support (Friedman 2014).

A just culture is critical to promoting a learning environment in which the providers report hazards, errors, and defects in care, without fear of blame or punishment. At our institution, providers are encouraged to check each other, be attentive to details and look for latent defects, speak up if concerned for safety, communicate clearly, escalate concerns along the chain of command if necessary, and maintain a questioning attitude. Such a culture breaks barriers such as hierarchy, interdisciplinary team dynamics, and fear of blame in the PICU. A just culture does not absolve individuals of any accountability but ensures that individuals are not blamed for systemic flaws that make it more likely for highly trained and dedicated providers to fail.

ICU informatics and quality improvement

Figure 3 illustrates a smart ICU model, where patient level data at the bedside are integrated and intelligently displayed, transforming them into actionable data for decision support. Modern informatics concepts must aim to utilise patient level data to ensure high quality care, continuous learning and quality improvement to impact patient outcomes. Such continuous bedside data allow learning from invaluable dynamic trends during illness course in the ICU, in context to therapies being applied. Automatic aggregation of data from a large number of patients, from multiple sites and via a variety of data sources has allowed the creation of large ICU databases such as the Multiparameter Intelligent Monitoring in Intensive Care II (MIMIC-II) research database (Saeed 2011). Examples of group learning using automatic or manually submitted data in small or large registries in the PICU population include the Virtual PICU systems (VPS), Pediatric Research Database (PRD Pivot) with rich de-identified data elements from the electronic health record, Pediatric Heart Network (PHN) collaborative learning model, Pediatric Cardiac Critical Care Consortium (PC4) clinical registry for infants and children in North American cardiac ICUs, Pediatric International Nutrition Study (PINS, I, II & III) database of nutritional intake and outcomes in mechanically ventilated

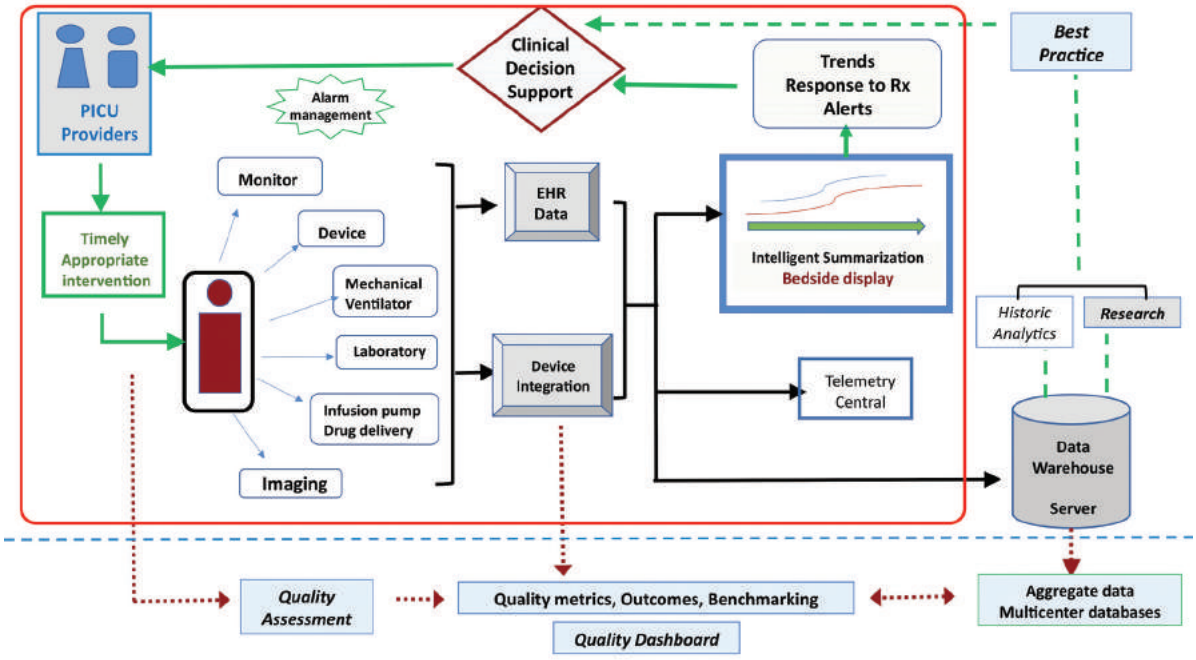


Figure 3. A Smart ICU model – leveraging patient-level and aggregate data for high quality care

children, Collaborative Pediatric Critical Care Research Network (CPCCRN) and Pediatric Emergency Care Applied Research Network (PECARN) databases, Society of Thoracic Surgeons Congenital Heart Surgery Database (STS-CHSD), Extracorporeal Life Support Organization (ELSO), Australia New Zealand Pediatric Intensive Care (ANZPIC) registry and the PICU International Collaborative Learning through Outcomes Data sharing (PICU-CLOUD) network.

Large patient-level datasets that can be leveraged for hypothesis generation, comparative effectiveness research, tracking, trending and benchmarking of ICU quality metrics, and a novel approach of collaborative learning. Attention to the accuracy, quality, and rigorous analyses of these data must be ensured, and data privacy, security, management, and governance are important considerations when sharing data across institutions on these digital platforms. Optimisation of electronic note writing, data input by nurses, alarm management to prevent fatigue, efficient storage, and analyses of data for research, intelligent data summarisation to provide decision support, are some of the benefits of healthcare IT advances. In order to benefit from these platforms, their development must take into account the unintended data overload, documentation burden, human behaviour expertise, and user interface in the PICU.

Collaborative learning

Best practices at the institutional level can be rapidly disseminated for wider adoption leading to improved patient outcomes. This concept is the central theme of collaborative learning, in which participating centres in a network share data and benchmark performances along key metrics. Potential target areas are explored for best practices using a collaborative multistep approach that involves site visits. Best practices are translated into clinical practice guidelines that are systematically applied across the network to examine their impact on clinical outcomes (Wolf 2016). The Pediatric Heart Network used a stepwise collaborative model that included data sharing, site visits to identify best practice, developing standards by consensus, and implementation of practice change across the network. They successfully decreased the time to extubation after paediatric cardiac surgery (Mahle 2016). Other examples of successful networks that leverage data for collaborative learning include the Children's Oncology Group, Cystic Fibrosis Foundation, and the Vermont-Oxford Collaborative.

QI Toolkit

A variety of tools have been developed to undertake systematic QI studies. Paediatric intensivists must become familiar with the methodologies and interpretation of the essential QI tools such as the i) Cause and effect (fishbone) diagram – to determine root causes of the event, ii) Failure Modes and Effects Analysis – to identify potential risks and their impact, iii) Flowcharts, Pareto charts, Run Charts and Control Charts – help visualisation of variation in performance over time, iv) Plan-Do-Study-Act rapid-cycle testing sheet to assess the impact of short iterative interventions. Details of these and other such tools are well described in the Institute for Healthcare Improvement (IHI) website (**ihi.org/resources/Pages/Tools/Quality-Improvement-Essentials-Toolkit.aspx**).

Quality metrics

Measurement is an important component of the healthcare transformation journey. Quality metrics are indicators that help measure PICU performance along agreed areas of importance to patient outcomes. These metrics allow serial examination of the unit performance over time, in the context of interventions, and are compared to internal goals or external (other PICU or group) benchmarks. QI metrics can

be process variables, outcome metrics or structural indicators. Characteristics of an ideal QI metric include a clear definition, measurable, show a degree of variability across sites such that good and poor performers can be differentiated, preferably an outcome measure or have a plausible link to the outcome of interest, not sensitive to severity of illness and reflect provider or unit performance. **Table 1** shows some examples of QI metrics in a PICU

Table 1. Examples of QI metrics in a PICU

Type	Metric
Outcome	Standardised Mortality Ratio (SMR) (Lower is better)
	MSICU Cardiac Arrest Rate (Lower is better)
	Survival to Hospital Discharge after Cardiac Arrest in the MSICU (Higher is better)
	Central Line-associated Bloodstream Infection (CLABSI) Rate (Lower is better)
	Catheter-associated Urinary Tract Infection (CA-UTI) Rate (Lower is better)
	Preventable Medication Error Rate (Lower is better)
Structure	Serious adverse event reporting system
	Vital equipment checks
	Nurse-patient ratio
	Infusion pumps – quality assessment and alarm management
Process	Hand Hygiene Compliance Rate (Higher is better)
	Medication Reconciliation Compliance (Higher is better)
	Daily rounding checklist compliance
	Extubation readiness testing
	Monitoring for delirium and sedation assessment
Patient/Family experience	Parent satisfaction around ICU cares
	Parent satisfaction around daily communication with providers

Safety culture in the ICU

The Michigan Keystone Project is a landmark effort that demonstrated the benefits of a collaborative QI approach to improve ICU outcomes. Over a 10-year period, sustained reductions in the rate of central line-associated bloodstream infections (CLABSI) were observed in over 100 ICUs across Michigan (Pronovost 2016). In addition to incorporating simplified best practices proven to reduce CLABSI, the investigators launched a systematic QI framework for preventing harm in the unit, embraced a strong safety culture, including checklists for safe central line insertion bundles, workflow re-design and empowering of providers to speak up for compliance to best practices. PICU leaders must encourage reporting of near misses and latent defect in the system without fear of reprisal. Near misses must be viewed as opportunities to learn about systems issues and potential improvements, rather than as evidence of safety. Vigilance for and anticipation of potential failures is a hallmark of a high reliability organisation.

Conclusions

Quality improvement in the ICU includes a spectrum of efforts aimed at improving individual patient experience and outcomes, leveraging smart technology and informatics to provide bedside decision support to deliver high-quality care, and the use of specialised tools to examine the impact of QI interventions on process and outcomes. PICU leaders must strive to transform their unit into a high reliability system by embracing a culture of safety, promoting continuous improvement, and investing in engineering a safer environemnt for patients and providers. A strategic quality management plan with broad stakeholder buy-in allows QI efforts in the PICU to be focused. Measurement, benchmarking and dissemination of performance metrics are essential to maintain provider engagement and sustain the improvements in processes and patient outcomes. ■

Conflicts of interest

None

Key points

- Paediatric intensive care unit is a highly complex environment with likelihood of for unintended patient harm.
- Quality improvement strategies aimed at improving patient outcomes must be firmly embedded in the PICU culture.
- PICU leaders must embrace the culture of high reliability and continuous quality improvement where every event or data point is considered an opportunity for learning. Providers in such units are preoccupied with failure, looking for defects in the system to prevent or mitigate harm
- Smart PICU designs allow providers to work in a safe and efficient environment, minimising harmful events and optimising patient comfort and experience
- Data management and intelligent summarisation facilitate bedside decision support in such units.
- Quality improvement tools allow gathering and intepretation of data, highlight opportunities for improvement, and facilitate collaborative learning that promotes high quality and value care in the ICU.

References

Friedman, C (2014) Toward Complete and Sustainable Learning Systems. Available from medicine.umich.edu/sites/default/files/2014_12_08-Friedman-IOM%20LHS.pdf.

Halpern NA (2014) Innovative designs for the smart ICU. Chest, 145(3):646-658

Hines S, Luna, K, Lofthus J, et al. (2008) Becoming a High Reliability Organization: Operational Advice for Hospital Leaders. (Prepared by the Lewin Group under Contract No. 290-04-0011.) AHRQ Publication No. 08-0022. Rockville, MD: Agency for Healthcare Research and Quality.

Institute of Medicine (2001) Crossing the Quality Chasm: A New Health System for the 21st Century. Washington, DC: The National Academies Press.

Mahle WT, Nicolson SC, Hollenbeck-Pringle D, Gaies MG, Witte MK, Lee EK, Goldsworthy M, Stark PC, Burns KM, Scheurer MA, Cooper DS, Thiagarajan R, Sivarajan VB, Colan SD, Schamberger MS, Shekerdemian LS (2016) Pediatric Heart Network Investigators. Utilizing a Collaborative Learning Model to Promote Early Extubation Following Infant Heart Surgery. Pediatr Crit Care Med, 17(10):939-947.

National Academies of Sciences, Engineering, and Medicine (2018) Crossing the global quality chasm: Improving health care worldwide. Washington, DC: The National Academies Press.

Pronovost PJ, Watson SR, Goeschel CA, Hyzy RC, Berenholtz SM (2016) Sustaining Reductions in Central Line-Associated Bloodstream Infections in Michigan Intensive Care Units: A 10-Year Analysis. Am J Med Qual, 31(3):197-202.

Saeed M, Villarroel M, Reisner AT, Clifford G, Lehman LW, Moody G, Heldt T, Kyaw TH, Moody B, Mark RG (2011) Multiparameter Intelligent Monitoring in Intensive Care II: a public-access intensive care unit database. Crit Care Med, 39(5):952-960.

Wolf MJ, Lee EK, Nicolson SC, Pearson GD, Witte MK, Huckaby J, Gaies M, Shekerdemian LS, Mahle WT (2016) Pediatric Heart Network Investigators. Rationale and methodology of a collaborative learning project in congenital cardiac care. Am Heart J. 174:129-137.

Walter Habenbacher
Vice President
CNSystems

feedback@cnsystems.com

www.cnsystems.com

Can Goal-Directed Therapy solve the economic burden of postsurgical complications?

How effective are less invasive or even noninvasive methods?

The clinical and economic burden of postsurgical complications and the economic impact of Goal-Directed Fluid Therapy (GDFT) implementation.

Improving the quality of care by reducing post-surgical complications, decreasing mortality, and decreasing hospital length-of-stay for surgical patients while also reducing cost, is a widespread goal of health services and healthcare professionals all around the world.

In recent years, innovative concepts, approaches, and technologies have been evaluated and recommended by renowned International Societies to achieve this goal. Among these concepts are Goal Directed Fluid Therapy (GDFT) strategies, which are defined as "*targeted haemodynamic and fluid management therapies using parameters such as stroke volume, cardiac output and oxygen delivery in conjunction with standard vital signs in managing patients during and immediately after surgery.*"[1]

While there are still debates going on about the best use, many clinical studies confirm the positive effect of GDFT on patient outcome after major surgery. The reduction of the most common complications, such as wound infection, sepsis or pneumonia, have been reported to result in a decrease of morbidity and even mortality in high-risk and intermediate-risk surgeries.[1,2,3] Nevertheless, the implementation of this approach in the clinical routine very often fails due to the perceived high cost for initial equipment.[1,2]

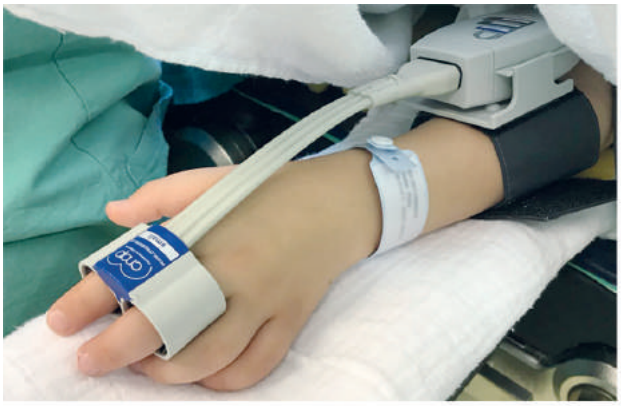
> **"with cost savings up to 77% on disposables, the noninvasive CNAP® technology can even be used in intermediate and low-risk surgeries"**

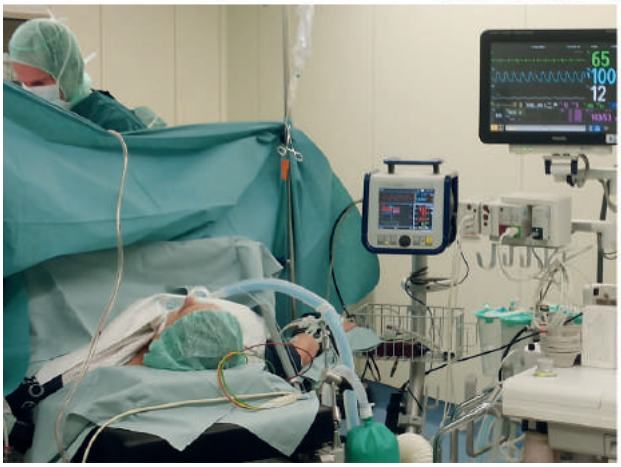
To obtain objective data, Manecke et al. "*assessed the clinical and economic burden of postsurgical complications in the American University Health System Consortium (UHC) in order to predict the economic impact of GDFT implementation.*" By comparing patients with and without postsurgical complications, they showed that out of 75,140 patients 8,421 developed one or more post-surgical complications, resulting in a morbidity rate of 11.2%.[1] "*In 2011 the UHC spent a total of $252 M to treat postsurgical complications in the study population.*"[1]

Apart from showing the dramatic impact of postsurgical complications on cost, the authors also calculated the savings potential of GDFT: "*After implementation of GDFT, projected gross savings would be $569-$970 per patient and $43-73 M for the entire UHC study population.*"[1] This implies savings of up to 29%, which easily compensate for the initial costs of the required equipment assuming approximately $300/patient.[1]

Patient benefit can be further expanded by using less invasive tools, which allow for the use of GDFT in a much wider patient population, including intermediate risk surgeries.[3] Less invasive or even noninvasive solutions are not only associated with less risks, but also with fewer complications for the patient than invasive methods. "*All of these issues are highly relevant for potential economic decision making.*"[2]

Using the noninvasive CNAP® Monitor in intermediate risk patients undergoing hip or knee replacement, Benes et al. showed that Goal-Directed Therapy based





on pulse pressure variation reduced postoperative wound infection, which is the number one complication and essential cost driver in surgical patients[1], by 61%.[3]

"The CNAP® Monitor was found to be comparable to its invasively assessing counterparts. Given these positive factors, the CNAP® device is already widely and routinely used in many clinical institutions; therefore our study could serve as a proof of concept for this praxis."[3] With cost savings up to 77% on disposables, CNAP® is definitely a promising solution to meet the demand for improved healthcare quality at low cost. ■

Key points

- Goal-Directed Fluid Therapy (GDFT) is defined as "targeted haemodynamic and fluid management therapies using parameters such as stroke volume, cardiac output and oxygen delivery in conjunction with standard vital signs in managing patients during and immediately after surgery."
- Many clinical studies confirm the positive effect of GDFT on patient outcome after major surgery.
- The implementation of this approach in the clinical routine very often fails due to the perceived high cost for initial equipment
- After the implementation of GDFT, gross savings easily compensate for the initial costs of the required equipment.
- With cost savings up to 77% on disposables, CNAP® is definitely a promising solution to meet the demand for improved healthcare quality at low cost.

References

[1] Manecke et al. (2014) Tackling the economic burden of post-surgical complications: would perioperative goal-directed fluid therapy help? Critical Care,18(5):566.

[2] Benes et al. (2014) Cost analysis of the stroke volume variation guided perioperative hemodynamic optimization - an economic evaluation of the SVVOPT trial results. BMC Anesthesiology,14(1):40.

[3] Benes et al. (2015) Fluid management guided by a continuous non-invasive arterial pressure device is associated with decreased postoperative morbidity after total knee and hip replacement. BMC Anesthesiology, 15(1):148.

Sapna Kudchadkar
Associate Vice Chair for Research
Anesthesiology and Critical Care Medicine
Associate Professor of Anesthesiology and Critical Care Medicine
Johns Hopkins University School of Medicine
USA

sapna@jhmi.edu

@SapnaKmd

PICU Up! A multicomponent early mobility intervention for critically ill children

An overview of the 'PICU Up!' mobility programme at Johns Hopkins Children's Center, which integrates sleep promotion, delirium prevention, and sedation optimisation to increase mobilisation in critically ill children.

What is the PICU Up! Programme?

Paediatric intensive units traditionally have had a culture where critically ill children are intubated and mechanically ventilated, immobilised, and highly sedated. This practice is primarily driven by a focus on safety and keeping children comfortable, along with the perception that bed rest provides greater haemodynamic stability. There is also the feeling that keeping children deeply sedated may ensure that the child does not remember their ICU stay, thus promoting the creation of a culture of immobility, which could have negative short and long-term implications for critically ill children.

The Paediatric Intensive Care Unit at Johns Hopkins is a 40-bed, tertiary care medical surgical unit that cares for children between the ages of 0 to 22 years. In 2011, our PICU team at Johns Hopkins began to think about how we were using the terms "sleep" and "sedation" interchangeably. For example, if a child already on an opioid and a benzodiazepine was agitated, we were giving them more medicine so that they would "sleep better." We know that sleep and sedation are very different states and can have an impact on the child's developing brain, but we weren't addressing the issue of restorative sleep in our patients whose brains are actively developing of children. A common misperception is that children in the PICU are older, but data from a recent multicentre study has demonstrated that more than half of our longer stay patients are under the age of two (park.web.jhu.edu). Therefore, we have an opportunity to positively impact neurocognitive development during a time that is most critical in a child's brain maturation.

When the PICU Up! Programme was being developed for Johns Hopkins, we decided to first address sleep as the "low-hanging fruit" because sleep is very disrupted for a number of reasons in the ICU, with modifiable risk factors. There is a great deal of discussion related to delirium in the adult literature, but we were only just starting to recognise it in paediatrics. Sleep disruption can be a risk factor for delirium.

> "mobilising children during the daytime and optimising their sleep at night was the best way to minimise exposure to opioids and sedative drugs and facilitate their functional recovery"

Over the years, the mortality rate in PICUs has declined quite significantly. The focus now has become not just survival, but survivorship. How does the child's stay in the PICU affect their life? For most children, their lives are very different when they go home then they were before they came to the PICU. They are weak, and their mobility is impaired. The quality of life they knew before PICU was different from the one after hospitalisation. PICU Up! was born out of all of those different issues.

When designing the core elements of PICU Up!, we had to create an overhaul in PICU culture. Our theory was that bed rest is bad and that mobilising children during the daytime and optimising their sleep at night was the best way to minimise exposure to opioids and sedative drugs and facilitate their functional recovery. These factors grounded the foundation of our PICU Up! programme strategy.

PICU Up! Champions

PICU Up was born out of engagement from a huge multidisciplinary group of champions from nursing, physical therapy (PT), occupational therapy (OT), respiratory therapy, child life specialists, nurse practitioners, and physicians. No additional staff was hired for this programme. We worked as a team to change our PICU culture to a culture of mobility instead of a culture of immobility. We outlined strategies to decrease sedation while keeping kids still safe and comfortable. And while we did this, we also addressed other issues that impact mobility, such as sleep hygiene and delirium. Together, we were able to create a structured programme to address each child's unique mobility needs, and championed setting a mobility goal for "Every kid, Every day." A major goal of our PICU Up! initiative was to get children and their families back into a routine as close to what they had at home.

PICU Up! Tiered System

PICU Up! is a three-level system - PICU up! Level 1, 2, and 3. There are objective clinical criteria for levelling the patients based on how sick they are, and where each level is connected with a set of interventions based on the needs of those children. The most criti-

Images provided by Johns Hopkins Children's Center.

cally ill patients would be considered Level 1, patients who are intubated with a high oxygen requirement, for example. As they start to get better or their clinical status improves, they move to Level 2. Level 2 generally includes patients who are on non-invasive mechanical ventilation or are intubated and getting close to extubation. Finally, Level 3 patients are on the launching pad for discharge to home or the inpatient floor, but still have critical care needs- these patients have the highest potential for mobilisation.

The purpose of creating the tiered system was to define the minimum requirements for children at each of those levels. We needed to make it clear to everyone that the goal was NOT to get every intubated kid up and out of bed and walking, but that there is an individualised spectrum of mobility for every child. We wanted every kid, every day to do the most that was possible, both safely and without overwhelming available resources. It was also important to change the way we thought about patients who were traditionally considered to be "too sick for therapy." Regardless of a child's severity of illness, almost always a therapy evaluation can offer something beneficial, even if those therapies don't start immediately. No patient is too sick for a physical or occupational therapy consultation, and our rehabilitation team appreciates being in the loop from the very beginning.

All patients at Johns Hopkins PICU get a PT or OT consult by day 3 of admission, and all of our patients have their sleep hygiene addressed and their routine set so that we're ideally not giving baths at 2am and not scheduling routine x-rays at 5 a.m. As patients progress, we start increasing their mobility, with an individualised mobility goal set for the day. The PICU Up! programme was implemented over a three-month period to demonstrate safety and feasibility. We collected a year of baseline pre-implementation data, implemented the programme over three months, and then looked at one year of post-implementation data. Our findings showed that the implementation of PICU Up! resulted in an increase in occupational therapy consultations and physical therapy consultations by day 3. The median number of mobilisations per patient by day 3 doubled, and more children were able to engage in mobilisation activities because of this intervention (Wieczorek et al. 2016). Twenty-seven percent of children ambulated by day 3, which was an increase of 15% pre-implementation. Among children 3 years or older, 20% ambulated prior to the implementation of the programme while 39% ambulated after implementation (Weiczorek et al. 2016).

Incorporating rehabilitation team consultation by day 3 made a huge difference, creating a culture where our nurses and our therapists were partnering together early in a child's course. The therapist isn't at the

Images provided by Johns Hopkins Children's Center.

bedside 24 hours a day, but the bedside nurse is. Therefore, it is really important for nurses to feel educated and empowered to facilitate mobility activities. Previous adult rehabilitation point-prevalence studies and emerging paediatric data are demonstrating just how crucial nursing engagement is for facilitating mobility.

It was also really important to involve family members in mobility because they obviously play a huge role in engaging their child. Since most of our patients are infants and toddlers, a major part of our mobility goals is to get children out of bed and to let them be held by their parents – I call it "therapeutic cuddles." That in itself is the daily mobility goal for many of our patients. PICU Up! has enabled us to completely change the culture of the unit to a unit of mobility and to ask questions that we've never thought to ask before. For example, there are infants in the PICU that have never been outside because they've lived in the hospital since they were born. We ask if a child can safely go outside with their parents and nurse. And if they can, our staff comes together to make it happen. Natural sunlight and outdoor time can also work wonders for older children and their families, not just physically but emotionally.

The new paradigm in our unit is to have patients who are minimally sedated and comfortable while avoiding continuous benzodiazepine infusions which have been shown to be an independent risk factor for delirium. Most of our patients receive a low dose of opioid to keep them comfortable with the noxious stimuli of the endotracheal tube, with a low-dose sedative as needed, usually dexmedetomidine. Some of our older patients do beautifully with patient-controlled analgesia, which gives them a feeling of control over their own pain management. Many of our patients participate in their care and communicate with their families and our staff, telling us what their needs are. Are there patients who still receive deep sedation? Yes- there will always be patients who must be deeply sedated to facilitate physiologic stability, but the major difference is that deep sedation is no longer the default.

Primary goals of PICU Up!

Ultimately, what we want to do is to use standardised, evidence-based interventions to increase each child's activity level in the PICU and to promote a culture of mobility. Our big picture goal is to normalise the child's routine as much as possible and optimise their functional outcome so they can go home to the best quality of life possible. Mobility, sleep hygiene, delirium prevention, and management, family engagement, and goal-directed sedation are all key components of PICU Up! and the Society of Critical Care Medicine's ICU Liberation 'ABCDEF' bundle. A recent multicenter study of 15,000 adults showed that ABCDEF bundle compliance was associated with a decrease in the duration of mechanical ventilation, mortality, and delirium (Pun et al. 2019). In the PICU, all five of these issues are intricately interrelated. If you're not sleeping at night, you're less likely to mobilise during the day. If you're not sleeping well, you're more likely to be delirious. If you're not mobilis-

ing, you're less likely to sleep well at night. If you're delirious and agitated, you're going to receive more sedation. If you're getting more sedation, you're more likely to be delirious. If your family is not engaged, you are less likely to mobilise. It's a vicious cycle, and all of these issues feed into each other. Therefore, the levels and the activities associated with each level incorporate all four of those things: sleep hygiene, delirium screening, early rehab, and goal-directed sedation. The multicomponent bundled intervention is bringing it all together so that people think of it as a PICU liberation approach as opposed to the sedation, delirium, and rehabilitation silos.

Types of activities for children in the PICU

Early mobilisation activities include in-bed activities such as passive range of motion, passive bed positioning, splinting, active range of motion, and active bed positioning. As patients progress, activities include motivating patients to sit on the edge of the bed, sit to stand, transfer, ambulate, and play (Wieczorek et al. 2016). Play is a key part of this programme. For babies, there's developmental play that is facilitated by our occupational therapists and child life specialists who bring in all sorts of unique items for the babies to play and engage with. The older children who can leave the unit can go to the rehab kitchen and bake cookies and brownies. They may not always be able to eat their baked goods, but they can always come back and distribute them to our staff! We also have riding and stationary bikes and portable treadmills for older children. Video games are an excellent way to facilitate dexterity for some of our older patients who aren't ready to get out of bed but can still use their hands.

Another key part of our rehabilitation initiative is our Augmented and Assistive Communication (AAC) programme. With more PICU patients awake and alert while intubated, we quickly realised we needed to give them more ways to communicate. Our child life specialists, occupational therapists, speech language pathologists, and nurses work together to identify a child's needs and create a communications plan with low-tech and high-tech devices. It may be as simple as a whiteboard or a board with pictures for them to point to; many of our older patients are writing, and can also use other devices like an iPad, and their families can also communicate with them. Several of our patients have texted with their friends, done homework to keep up at school, and use video chat to communicate with family when they are not at the bedside. Even for children who do not survive their PICU stay, facilitating communication can be priceless for patients and families at the end of life.

Mobility and the sedated child

For children who require deep sedation, we get our rehabilitation team to the bedside as soon as possible and make sure that we're doing as much as possible while they're sedated to prevent morbidity. For other patients, we optimise active engagement in mobility which has changed how much sedation they need. Increased activity during the day means less delirium and improved circadian rhythms. There's no question that the PICU Up! programme has helped decrease sedative and opioid use among PICU patients, and we are actively studying these outcomes.

Wider implementation of PICU Up!

We want to facilitate the implementation of multicomponent mobility programmes as widely as possible to decrease the need for PICUs to "reinvent the wheel." PICU Up! is already being implemented in several other PICUs in the United States including the Cincinnati Children's Hospital, Northwestern Lurie Children's Hospital, University of Virginia, Vidant Hospital in North Carolina and St. Jude Children's Hospital. Every year we host about 150 multidisciplinary team members who come to learn specifically about paediatric critical care rehabilitation implementation at the Annual Johns Hopkins Critical Care Rehabilitation Conference (bit.ly/icurehab). If a PICU wants to license our programme, we can make that happen. Or if they want to create and implement their own programme, we are here to help. The goal is to ensure that a culture of mobility is disseminated safely and effectively. We have six other ICUs that are set to implement the programme within the next year as part of a multicentre, randomised controlled trial (**clinicaltrials.gov/ct2/show/NCT03860168**).

Future Plans

First, we need to demonstrate that programmes like PICU Up! have an impact on both short and long-term patient outcomes. The natural next step is then to start to hone in more on the mechanisms by which our interventions are working and to determine the appropriate dose, frequency, and duration of rehabilitation for critically ill children. We also want to determine what activities are the most beneficial for which patients, and how often should we be doing them moving forward. It's important for children to be able to get back to the lives they had before their critical illness as quickly as possible. We need to ask if these children, once discharged from the PICU, are sleeping differently when they go home? Are we making a difference in their long-term sleep patterns and sleep trajectory? What are the underlying mechanisms by which all of these interventions are working so that we can continue to understand more on a patient-based level and can optimise outcomes for every child in the PICU? There is much work to do. ■

Key points

- The primary goals of the PICU Up! programme include increasing mobility, normalising the child's routine, optimising their functional outcome, optimising sleep hygiene, and decreasing exposure to sedative and interventions with medications.
- PICU Up! was made possible by engagement from a huge multidisciplinary group of champions.
- PICU Up! is a tiered system that uses objective clinical criteria for levelling patients based on their severity of illness.

References

PARK-PICU. Prevalence of acute rehab for kids in the PICU. Available from park.web.jhu.edu/

PICU Up!: Trial of a Multicomponent Early Mobility Intervention for Critically Ill Children (PICU Up!). Available from clinicaltrials.gov/ct2/show/NCT03860168

Pun BT, Balas MC, Barnes-Daly MA, Thompson JL, Aldrich JM, Barr J, Byrum D, Carson SS, Devlin JW, Engel HJ, Esbrook CL, Hargett KD, Harmon L, Hielsberg C, Jackson JC, Kelly TL, Kumar V, Millner L, Morse A, Perme CS, Posa PJ, Puntillo KA, Schweickert WD, Stollings JL, Tan A, D'Agostino McGowan L, Ely EW (2019) Caring for Critically Ill Patients with the ABCDEF Bundle: Results of the ICU Liberation Collaborative in Over 15,000 Adults. Critical Care Medicine, 47(1):3-14.

Wieczorek B, Ascenzi J, Kim Y, Lenker H, Potter C, Shata NJ, Mitchell L, Haut C, Berkowitz I, Pidcock F, Hoch J, Malamed C, Kravitz T, Kudchadkar SR (2016) PICU Up!: Impact of a Quality Improvement Intervention to Promote Early Mobilization in Critically Ill Children. Pediatr Crit Care Med, 17(12):e559–e566.

CARING FOR THE CRITICALLY ILL CHILD

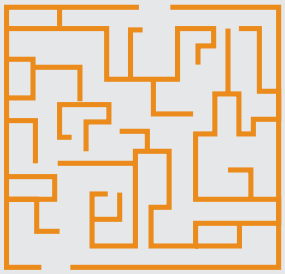
PICUs – KEY FACTS

- Paediatric Intensive Care Units (PICUs) occupy a central position in the care of hospitalised children.
- Approximately 200 children per 100,000 require hospitalisation in PICUs because of serious illness.
- Nearly 90% of paediatric deaths occur in neonatal and paediatric intensive care units.
- Most deaths in the PICU are preceded by withdrawal of mechanical ventilation.

Sources: Kanwaljeet, A (2014) Front Pediatric 2:35.
Doorenbos et al. (2012) J. Soc Work End Life Palliat Care, 8(4): 297–315.

CHALLENGES FOR PICU PATIENTS AND SURVIVORS

- Reduced physical function
- Delayed recovery
- Cognitive decline
- Feeding disorders
- Functional impairments
- Psychological stress
- Reduced quality of life



Source: Walker and Kudchadkar (2018) Translational Pediatrics, 7(4): 308–313.

CRIPPLING EFFECTS IN PICU PATIENTS

- ICU-acquired weakness
- Delirium
- Pain
- Agitation

Source: Walker and Kudchadkar (2018) Translational Pediatrics, 7(4): 308–313.

ICU LIBERATION COLLABORATIVE

ICU liberation collaborative is a campaign designed to create lean, sustainable, and highly functioning ICU teams that work with patients and families to create a safe and comfortable patient environment by implementing the Pain, Agitation, and Delirium (PAD) guidelines utilising the ABCDEF bundle.

Source: Society of Critical Care Medicine (sccm.org/ICULiberation/About)

TOP REASONS FOR CONFLICTS IN PICU

60%	Conflicts between healthcare and family
48%	Poor communication
39%	Unavailability of a parent/guardian
39%	Disagreements over the child's care plan
21%	Coping problems
12%	Dysfunctional families
9%	Conflicts about decision making
6%	Young parents

Source: Doorenbos et al. (2012) J. Soc Work End Life Palliat Care, 8(4): 297–315.

COMPONENTS OF THE ABCDEF BUNDLE

A	Assess, Prevent and Manage Pain
B	Both Spontaneous Awakening Trials (SAT) and Spontaneous Breathing Trials (SBT)
C	Choice of Analgesia and Sedation
D	Delirium: Assess, Prevent and Manage
E	Early Mobility and Exercise
F	Family Engagement and Empowerment

Source: Society of Critical Care Medicine (ccm.org/ICULiberation/ABCDEF-Bundles)

PICU-acquired complications: the new marker of the quality of care

Karen Choong
Professor, Department of Pediatrics and Critical Care
Department of Health Research Methods, Evidence and Impact
McMaster University, Ontario, Canada

choongk@mcmaster.ca

@karen_choong

This article describes the rise in PICU-acquired morbidities and its impact on patient outcomes. It discusses early rehabilitation strategies to improve patient outcomes in PICU.

Introduction

Critical care has traditionally been focused on early recognition of life-threatening conditions, resuscitation, and stabilisation of organ dysfunction, and ultimately improving mortality. Our ability to deliver critical care and advanced life support has continued to improve over the last two decades, and as a result, mortality rates in children admitted to Paediatric Intensive Care Units (PICUs) have fallen significantly to an all-time low of 1- 3% in developed nations (Burns et al. 2014; Hartmann et al. 2017; Namachivayam et al. 2010). Increased survival amongst critically ill children has resulted in the following consequences: Firstly, a population shift. Patients admitted to PICUs today are sicker and more complex. Critically ill children with pre-existing chronic co-morbidities have risen significantly; these patients now constitute 53-68% of the PICU population (Choong et al. 2018; Pinto et al. 2017). This group of patients has a significant impact on PICU practice and resources. They require the majority of our invasive therapies; they occupy the longest duration of stay, and they consume 81% of costs within the PICU (Briassoulis et al. 2004; Rennick and Childerhose 2015). Furthermore, they are our future patients; 35% of these children are readmitted to the hospital within 6 months following PICU discharge (Choong et al. 2018). The second consequence of improved survival amongst critically ill children is a significant rise in PICU-acquired complications (PACs) amongst survivors (Pollack et al. 2014). The incidence of PACs has risen dramatically, and now far exceeds mortality. PACs are undesirable and unintended sequelae, distinct from the admission diagnosis, and acquired during their course of a child's PICU stay. Specifically, these include but are not restricted to iatrogenic withdrawal, delirium, and PICU-acquired weakness.

> "the majority of critically ill children are excessively sedated, and prolonged bed rest is a common practice in PICUs"

The rise of PICU-acquired complications

The traditional practice in many PICUs is to sedate, restrain and immobilise critically ill children as they are often considered "too sick to move" (Choong et al. 2013). Subsequently, the majority of critically ill children are excessively sedated, and prolonged bed rest is a common practice in PICUs (Choong et al. 2013; Choong et al. 2014; Garcia Guerra et al. 2016). This paradigm, along with a lack of clinician awareness of harmful sequelae (Long and Williams 2016), has led to an increase in the following specific PACs in the last 10 years: iatrogenic withdrawal syndrome has risen from 17 to 57% (Anand et al. 2010; LaRosa and Aponte-Patel 2019), delirium has increased from 10% to 25% overall and affects as many as 53% of mechanically ventilated children (Traube et al. 2017; Creten et al. 2011). PICU-acquired weakness, which less than a decade ago affected only 2%, now affects as many as 23% children (**Table 1**) (Choong et al. 2018; Kukreti et al. 2014). These morbidities are inter-related. Sedation depresses respiratory effort and prolongs mechanical ventilation; it hinders mobility and increases the risk of delirium and iatrogenic drug withdrawal (Silver et al. 2015; Ista et al. 2007). Immobility during critical illness causes neuromuscular atrophy and weakness (Koo et al. 2011), it exacerbates pain and agitation, further perpetuating the cycle of sedative administration. Immobility is also an independent risk factor for delirium (Vet et al. 2013; Kudchadkar et al. 2014). Sleep is commonly disrupted in critically ill patients, due to numerous factors such as a disruptive environment, invasive interventions, interruptions for nursing care, pain related to the underlying illness and pharmacological interventions (Kudchadkar et al. 2014). Sleep disruption results in delirium and insomnia, in addition to impaired immunity, catabolism, and respiratory compromise. Over-sedation, delirium, and weakness are therefore not distinct critical illness complications (**Figure 1**). Their pathogeneses are interrelated, and they lead to common adverse short and long-term outcomes (Vasilevskis et al. 2010). PACs are common; 61% of critically ill children develop one or more PACs (Choong et al. 2018). PACs are important to clinicians as well as patients; they are strongly associated

with prolonged mechanical ventilation, longer hospitalisation, and higher mortality (Kukreti et al. 2014; Ista et al. 2007; Traube et al. 2017). The development of one or more of these PACs is associated with an increased risk of poor functional recovery, poor quality of life, persistent neurocognitive and psychological sequelae, and increased parental stress following PICU discharge (Choong et al. 2018). Collectively these constitute the post-intensive care syndrome which we now understand affects a significant proportion of paediatric survivors and their families, as it does critically ill adults (Watson et al. 2018).

Safety priorities and knowledge gaps

Despite its increasing incidence, PACs continue to be under-recognised amongst PICU clinicians. Sedation is often prioritised over awakening and mobilisation, as key safety concerns are most commonly focused on preventing unplanned extubation (da Silva et al. 2008). Clinicians are comfortable with sedating patients, but are often uncomfortable with mobilisation, and allowing children to awaken (Long and Williams 2016; Treble-Barna et al. 2019). Clinicians therefore often have conflicting attitudes towards sedation – we understand the potential side effects, yet we express the desire for more sedation for our patients (Flaigle et al. 2016). Further challenges faced by PICU clinicians is that the majority of intubated children are infants and toddlers or because of developmental disabilities, are non-verbal. Movement and wakefulness in these children are therefore often interpreted as agitation and the need to escalate sedation. Benzodiazepines and opioids are subsequently administered to facilitate sleep, but to the contrary, these medications decrease restorative sleep and increase arousal frequency, leading to further agitation and deterioration in sleep quality (Kudchadkar et al. 2014). Many PICU physicians admit not recognising nor understanding how to assess for delirium in children (Long and Williams 2016). There is a lack of awareness that critically ill children are at significant risk of delirium, and that sleep disruption is extremely common (Garcia Guerra et al. 2016; Kudchadkar et al. 2014). Subsequently, there is a paucity of routine monitoring for delirium and non-pharmacological sleep promotion in PICUs worldwide (Kudchadkar et al. 2014).

In summary, the rise in PICU-acquired complications are not only due to increasing complexity and co-morbidities amongst the critically ill paediatric population, but in large part attributable to a traditional practice paradigm of excessive sedation, prolonged immobility, knowledge gaps with respect to the risk of our current practice and subsequently, a lack of standardised strategies for the monitoring of and prevention of these sequelae.

Table 1: PICU-acquired complications

PICU-acquired complications	Rate
Increasing incidence	
Iatrogenic Withdrawal[14]	57%
Delirium[15]	25%
PICU-acquired weakness[4]	23%
Decreasing incidence	
Unplanned extubation[34]	0.5/100 ventilator days
Central line associated blood stream infection[52,53]	0.7-1.0/1000 catheter days
Pressure injury[54]	3.7/1000 patient days

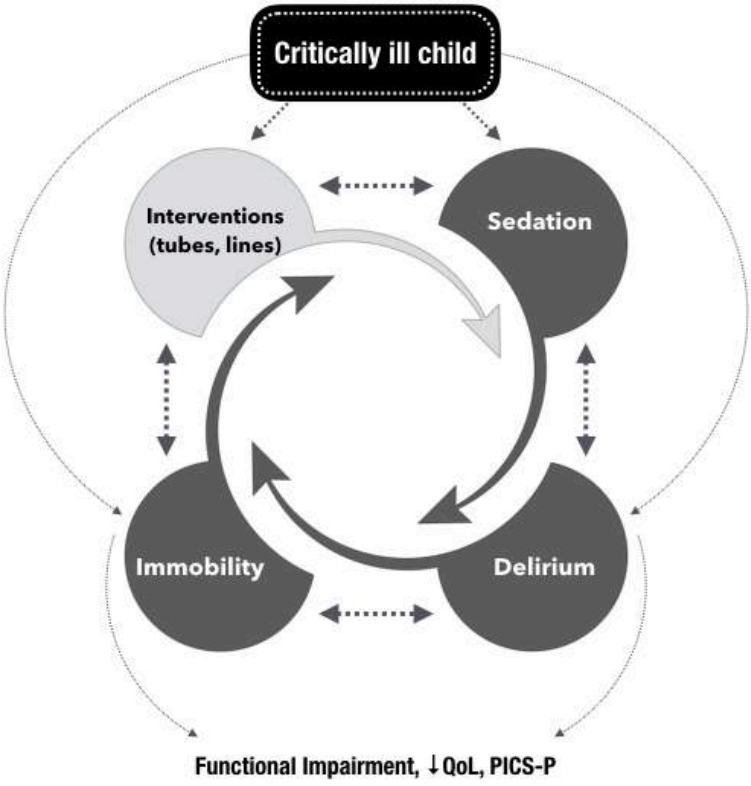


Figure 1. Common pathogenesis and sequelae of PICU-acquired complications.
Figure modified with permission from Vasilevskis et al. (2010) Chest.

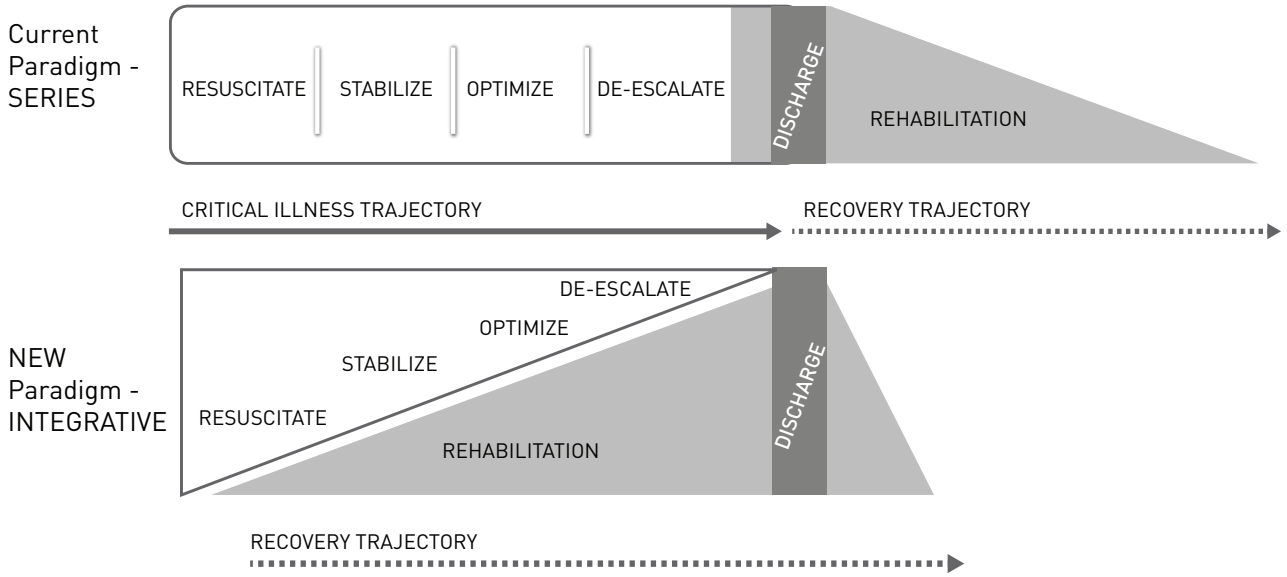


Figure 2. Paradigm shift, from a "series" to an "integrative" model, where rehabilitation is considered early, rather than the end of the critical illness trajectory.

Harm reduction and quality improvement

As the majority of critically ill children survive, mortality is no longer the most appropriate quality indicator of our care (Goodacre et al. 2015). Quality of life and function are now recognised as more meaningful and prioritised outcomes for patients and families (Merritt et al. 2018). PACs are common and harmful, but preventable, and therefore represent an opportunity for patient-centred, quality improvement in the PICU (Choong et al. 2018). As PACs impact long-term patient outcomes, reducing PACs may therefore not only improve PICU outcomes, but optimise functional recovery post-PICU discharge.

As over-sedation, withdrawal, delirium, and immobility are inter-related, single-pronged, independent interventions may not be the most effective approach to improve a common end-point of functional recovery (Craig et al. 2008). This may in part explain the lack of efficacy in previous studies targeted only at sedation or early mobilisation in isolation (Vet et al. 2016; Curley et al. 2015; Morris et al. 2016). Rather than providing different solutions to the same problem, addressing PACs collectively through a bundle of complementary quality improvement interventions enhances uptake and promotes multi-disciplinary team collaboration (Dixon-Woods et al. 2012). Promoting early rehabilitation as harm reduction emphasises the importance of reducing ICU-acquired morbidities in optimising functional outcome and quality of life in critically ill patients. Implementing ICU-based rehabilitation through an "ABCDEF"

> **"sedation is often prioritised over awakening and mobilisation, as key safety concerns are most commonly focused on preventing unplanned extubation"**

Bundle is currently a topic of much research in critical care, and has been demonstrated in adults to significantly improve symptom-related outcomes such as the duration of mechanical ventilation, coma and delirium, as well as improved system and patient-related outcomes such as survival, hospital discharge and ICU readmission rates (Pun et al. 2018). Furthermore, there appears to be a dose-response relationship between higher proportional bundle performance and improvements in these outcomes. With respect to the evidence for PICU-based rehabilitation the current evidence suggests that less is more: less sedatives, less benzodiazepines, and less immobilisation may reduce the length of hospital stay, reduce the risk of delirium, and improve adaptive functional outcomes (Fink et al. 2019; Mody et al. 2018; Simone et al. 2017; Penk et al. 2018). Minimum, effective sedation and analgesia has been shown to be safe, enables spontaneous breathing, improves sleep, reduces withdrawal and facilitates earlier mobilisation (Kudchadkar et al. 2014; Curley et al. 2015). Early mobility-based rehabilitation is feasible and safe in critically ill children (Choong et al. 2017; Cuello-Garcia et al. 2018). Implementing PICU-based early rehabilitation has been shown in preliminary studies to improve the time to and duration of mobilisation (Fink et al. 2019; Choong et al. 2017). Importantly, employing a rehabilitation bundle improves the unit culture through improved family engagement team collaboration and communication (Kawai et al. 2018; Costa et al. 2018). Whether an early rehabilitation bundle leads to improved short and longer-term patient important outcomes in critically ill children is a subject of ongoing research (Choong et al. ongoing research).

Early PICU-based rehabilitation, shifting the paradigm

While applying an ABCDEF bundle addresses PACs collectively, implementing PICU-based rehabilitation is complex and requires significant education, team collaboration, institutional buy-in, and continuous audit and feedback mechanisms to ensure sustainability (Balas et al. 2019). No longer is the critical care clinician's responsibility restricted to early recognition of clinical decompensation, resuscitation and improving survival, as the majority of children survive their critical illness. These patients are our future patients; we have a responsibility to our survivors to improve their survivorship, beginning within the PICU, to beyond the PICU. Creating a culture of practice begins with education and increasing awareness of PACs. Emerging paediatric-specific evidence highlighting the common incidence and source of key modifiable PACs is an important first step to raising awareness not just amongst clinicians, but to patients and families. Education should be targeted at paying equal attention and efforts to prevent common PACs, as we do to those that are infrequent (**Table 1**). Implementing ICU-based rehabilitation therefore requires a paradigm shift from considering the critical illness trajectory in series where rehabilitation is traditionally reserved to the "back end" of critical care, to an integrative model where rehabilitation is considered early in the critical illness trajectory as an important part of front-end care (**Figure 2**). An integrative model may provide us with the best opportunity to screen for and reduce morbidity prior to the onset of PACS, and in so doing, optimise functional recovery. Understanding and improving ICU survivorship is a key focus of ongoing adult and paediatric critical care research, prompting novel interventional, quality improvement and implementation science research methods (Choong et al. ongoing research; Wieczorek et al. 2016; Nydahl et al. 2018), as well as international collaboratives in identifying core patient and family-centred outcomes, and patient and family engagement in critical care research (Needham et al. 2017; Connolly and Hough 2017).

Conclusion

The success of paediatric critical care is evidenced by significant improvements in patient survival. However, these improvements are offset by the emergence of PICU-acquired morbidities both in the short term, as well as persistent long-term patient and family sequelae. Markers of success in critical care can therefore no longer be measured by survival, but improvements in longer-term survivorship post-PICU discharge. Improved understanding of populations shifts within the PICU, increasing awareness of PACs and the post-intensive care syndrome have offered us opportunities to highlight the importance of harm reduction, education and knowledge translation around survivorship following critical illness. A paradigm shift from early recognition and resuscitation, to early recognition and the introduction of ICU-based rehabilitation strategies, may offer us opportunities to reduce harm, improve the process of care, facilitate patient and family engagement team collaboration in clinical care and critical care research, and most importantly, improve functional recovery and quality of life following critical illness.

Disclosures

Karen Choong has received funding from the Academic Health Sciences Alternate Funding Plan Innovation grant to conduct the Early Rehabilitation in Critically Ill Children (PICU Liber8) Study. (Funding reference #: HAH-17-04). ■

Key points

- Mortality rates in children admitted to Paediatric Intensive Care Units (PICUs) have fallen significantly to an all-time low of 1- 3% in developed nations.
- Critically ill children with pre-existing chronic co-morbidities have risen significantly; these patients now constitute 53-68% of the PICU population.
- Sleep is commonly disrupted in critically ill patients, due to numerous factors such as a disruptive environment, invasive interventions, interruptions for nursing care, pain related to the underlying illness and pharmacological interventions.
- Despite its increasing incidence, PACs continue to be under-recognised amongst PICU clinicians.
- The rise in PICU-acquired complications are not only due to increasing complexity and co-morbidities amongst the critically ill paediatric population, but in large part attributable to a traditional practice paradigm of excessive sedation, prolonged immobility, knowledge gaps with respect to the risk of our current practice and subsequently, a lack of standardised strategies for the monitoring of and prevention of these sequelae.

References

Anand KJ, Willson DF, Berger J, et al.(2010) Tolerance and withdrawal from prolonged opioid use in critically ill children. Pediatrics, 125(5):e1208-1225.

Briassoulis G, Filippou O, Natsi L, Mavrikiou M, Hatzis T et al (2004) Acute and chronic paediatric intensive care patients: current trends and perspectives on resource utilization. QJM, 97(8):507-518.

Burns JP, Sellers DE, Meyer EC, Lewis-Newby M, Truog RD et al. (2014) Epidemiology of death in the PICU at five U.S. teaching hospitals. Crit Care Med,42(9):2101-2108.

Choong K, Fraser D, Al-Harbi S, et al. (2018) Functional Recovery in Critically Ill Children, the "WeeCover" Multicenter Study. Pediatr Crit Care Med, 19(2):145-154.

Choong K, Koo KK, Clark H, et al. (2013) Early Mobilization in Critically Ill Children: A Survey of Canadian Practice. Crit Care Med, 41(7):1745-1753.

Choong K, Foster G, Fraser DD, et al.(2014) Acute rehabilitation practices in critically ill children: a multicenter study. Pediatr Crit Care Med, 15(6):e270-279.

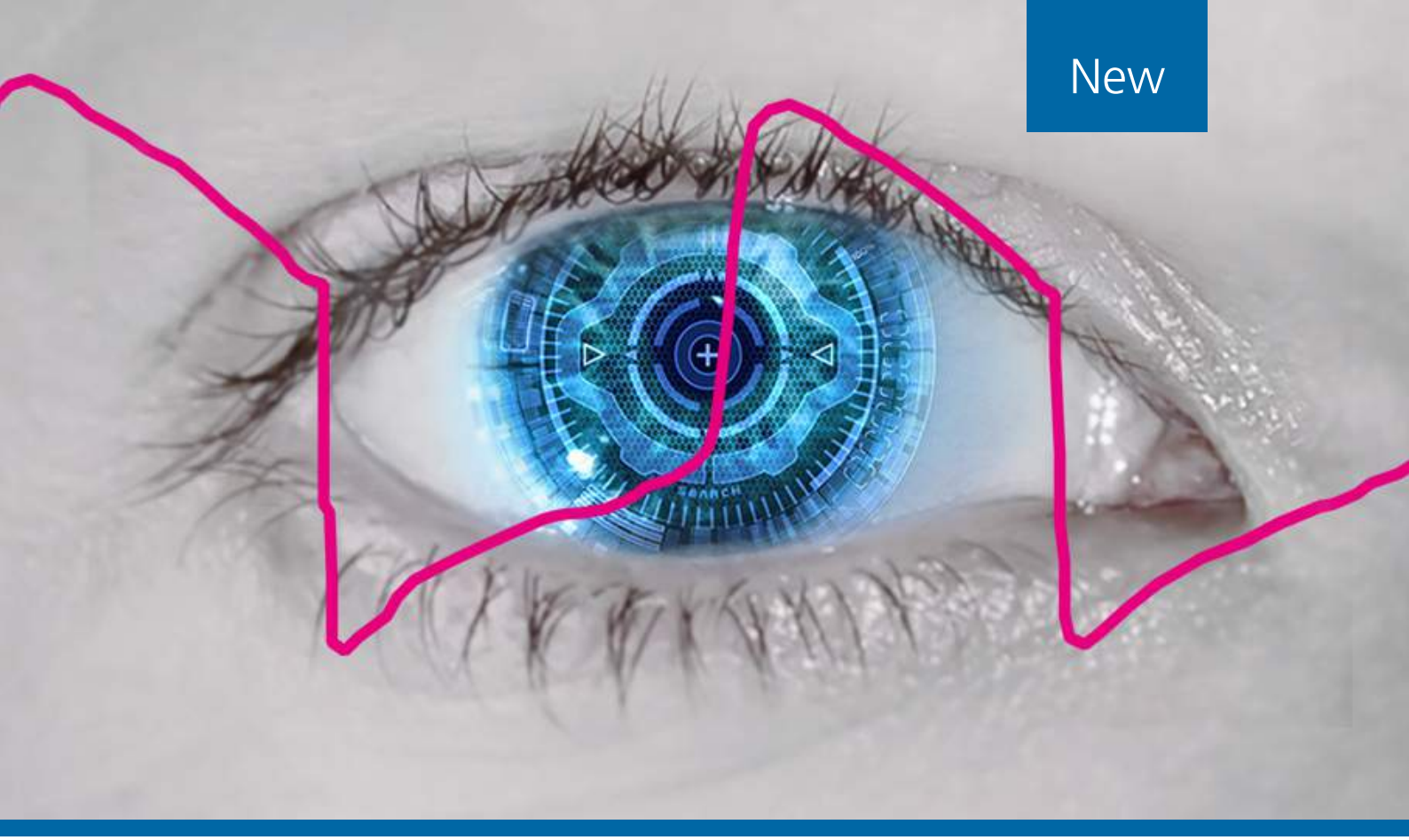
Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M et al. (2008) Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ, 338:a1655.

Creten C, Van der Zwaan S, Bankespoor R, Leroy P, Schieveld J et al. (2011) Pediatric delirium in the pediatric intensive: a systematic review and an update on key issues and research questions. Minerva Anesthesiol, 77:1099-1107.

da Silva PS, de Aguiar VE, Neto HM, de Carvalho WB et al. (2008) Unplanned extubation in a paediatric intensive care unit: impact of a quality improvement programme. Anaesthesia, 63(11):1209-1216.

Dixon-Woods M, McNicol S, Martin G. et al. (2012) Ten challenges in improving quality in healthcare: lessons from the Health Foundation's programme evaluations and relevant literature. BMJ Qual Saf, 21(10):876-884.

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



IntelliSync+

Keeping an eye on patient-ventilator synchrony

- ✓ For invasive or noninvasive ventilation modes
- ✓ During inspiration and expiration
- ✓ Noninvasive method
- ✓ No additional hardware or accessories required

www.hamilton-medical.com/intellisync+

HAMILTON MEDICAL

Intelligent Ventilation since 1983

Elisabeth Esteban
Pediatric intensivist
Head of the Pediatric Transport Team
Pediatric Intensive Care Unit
Hospital Sant Joan de Déu, Barcelona, Spain

eesteban@sjdhospitalbarcelona.org

Iolnda Jordan
Pediatric intensivist
Pediatric Intensive Care Unit
Hospital Sant Joan de Déu, Barcelona, Spain

ijordan@sjdhospitalbarcelona.org

Francisco José Cambra
Head of the Pediatric Intensive Care Unit
Hospital Sant Joan de Déu
Barcelona, Spain

fjcambra@sjdhospitalbarcelona.org

Caring for children in the PICU

From novel technology to family-centred care: new challenges for old needs.

Challenges and opportunities to improve care and practice in the PICU.

"Martin, 2 years old. Sepsis and pneumoniae. High monitoring systems and modern therapies. A nurse is talking to his parents. A smile and a kind gesture help them in this overwhelming experience. Fear and hope." This is only an instant picture from a Paediatric Intensive Care Unit (PICU) to illustrate the challenge of critical children care: the fusion of advanced medicine and emotional care.

In the next paragraphs, we will summarise current challenges and opportunities to be addressed in order to improve our practice in the PICU.

Introduction

PICUs have experienced an increase in activity and complexity in the recent decades. Clinical practice has improved dramatically due to new monitoring systems and technological advances in diagnosis and treatment.

Acute medical conditions such as infections, respiratory diseases, injuries, and high complexity surgeries are the most common reasons for admission. Chronic patients often need critical care because of rapid deterioration. Oncological patients frequently require intensive care, and that represents a challenge.

In the era of precision medicine, we highlight the interesting review of Professor Jean Louis Vincent (2019), "treating individuals rather than diseases will necessitate a paradigm change in our approach to diagnosis and management." This change will not be different in PICU. Not all treatments will be adjusted to all patients. Molecular-based targeting of treatments is currently used in other fields such as oncology and, probably in the future, we will use it to personalise therapy in paediatric critical care.

Mortality in PICU is markedly lower than in adult units, according to figures that vary depending on the country and the allocated resources. Mc Crory et al. (2017) reported a 2.31% mortality rate in the United States and Rashma et al. (2018) reported a 10.58% mortality rate in a PICU in India.

Regarding emotional disturbances, admission into a PICU causes psychological distress for the patients and their families because of the emotional intensity they experience. A family-centred model is essential to provide the best care for children. We will overview the current challenges of managing children in the PICU towards excellence in all fields.

The latest advances on diagnosis and therapy

Moving towards a personalised medicine model is facilitated by recent technology breakthroughs that promote a more accurate management of patients in PICU. Smart PICUs using Big Data predictive analysis including intelligent infusion systems will reduce administration errors (Manrique-Rodriguez et al. 2019), and decision making will be facilitated.

New diagnostic tests or techniques, such as rapid pathogen identification, are decisive in facilitating the choice of the most adequate therapy. Real-time PCR tests to diagnose aetiology and resistance in children with infectious diseases can be a useful tool that can provide additional information for clinical decision making. Current PCR tests are showing promising results in children (Papan et al. 2017; Gowin et al. 2017).

Biomarkers are used as complementary data in the overall assessment of the patient, but in the near future, they could play a key role in defining more precisely the true pathology. In this scenario, biomarkers will be crucial to achieving more targeted therapies according to a molecular-based approach, as Yehya (2019) suggested in an interesting editorial.

Regarding new treatments, novel therapies for oncologic patients have increased the number of "new" patients in our units. As an example, we could mention the case of the chimeric antigen receptor (CAR) T-cell therapy for refractory B-cell acute lymphoblastic leukemia that has led admissions to PICU in order to be treated from the resulting inflammatory response generated (Foster and Maude 2018). These patients are a good

Figure 1. PICU Hospital Sant Joan de Déu, Barcelona

example of personalised therapy based on pathophysiology. This therapy has opened a line of treatment for other leukaemia and solid tumours.

There are many new advances being incorporated in the PICU: ECMO, non-invasive ventilation, neutrally-adjusted ventilator assistance, new treatments for recipient of transplants, ventricular assistant devices, neuromonitoring, epilepsy surgery, etc. Future challenges such as the use of 3D impression, the management of emerging infections as Ebola or dengue, multidrug-resistant infections, or immunotherapy will be faced.

All these advances require continuous training of specialised staff, therefore institutions must provide professionals the opportunity for continuous improvement.

Humanisation in the PICU

In our opinion, the field where PICUs have experienced their greatest transformation is in the humanisation of assistance. This cultural change in healthcare mindset is becoming more challenging to professionals than learning and managing new techniques or the latest therapies. In consequence, a major implication and commitment will be required, becoming both a challenge and an opportunity.

The stay in the PICU becomes a stress and anxiety generator for parents. A few years ago, and still now in some cases, parents were allowed to visit their children briefly. Nowadays, most PICUs promote 24-hours access, with clear benefits to children, families, and professionals. In addition, changes in the physical environment of the PICUs have been performed advocating for private rooms instead of the classical open floor units. Our PICU, in Hospital Sant Joan de Déu, Barcelona, has recently shifted from shared rooms to private rooms (**Figure 1**). This experience has been a challenge with benefits in terms of infection prevention, privacy, decrease of environmental stress and noise. Families can now sleep in the room with their child, hence reducing the fatigue they experience. The main challenge has been the adaptation to a new model where the nurses work in the patient's box without the previous physical signals and awareness elements indicating the status of other patients and nurses. The concern for patients' safety in the implementation of this model has been resolved by using a portable alarm system that allows nurses to be permanently aware of patients' status and easily assist fellow colleagues in case of warning signals.

> "a family-centred model is essential to provide the best care for children"

Programmes focused on improving the hospitalisation experience can be adapted to the PICU. Music therapy, clowns, art or animal therapy have been successfully used in the PICU setting, and it is fair to highlight that these programmes have also had a positive effect on parents' experience.

All these changes are included in the family-centred care (FCC) model that promotes the involvement of families in the care of their children. This approach, which has been endorsed by major professional organisations, can deeply influence clinical decisions and patient outcomes (Meert et al. 2013). The American Academy of Pediatrics (AAP) defines FCC as "an innovative approach to the planning, delivery, and evaluation of health care that is grounded in a mutually

Table 1. American Association of Pediatrics core principles of family-centred care

1	Listening to and respecting each child and their family
2	Ensuring flexibility in organisational policies, procedures, and practices
3	Sharing complete, honest, and unbiased information with patients and families
4	Providing and ensuring formal and informal support for the child and family
5	Collaborating with patients and families at all levels of health care
6	Recognising and building on the strengths of individual children and families

Data from American Academy of Pediatrics, Committee on Hospital Care and Institute for Patient- and Family-Centered Care. Patient- and family-centred care and the paediatrician's role. Source: Pediatrics

Table 2. ABCDEF bundle to promote early mobilisation

A	Assess, prevent and manage pain
B	Both spontaneous awakening trial and spontaneous breathing trial
C	Choice of analgesia and prevention
D	Delirium, assessment, prevention and management
E	Early mobility and exercise
F	Family engagement and empowerment

The ABCDEF bundle: science and philosophy of how ICU liberation serves patients and families. Source: Critical Care Medicine

beneficial partnership among patients, families, and providers that recognises the importance of the family in the patient's life" (AAP 2012). The PCC is based on six core principles that are listed in **Table 1**. Currently, FCC is considered the gold standard of care in paediatrics (Ramenzani et al. 2014); however, its implementation can be a challenge when the child is unstable. Nurses play a crucial role in the implementation of FCC. Coats et al. (2018) have recently published the nurses' reflections on the benefits of FCC in PICU. Nurses must be involved in the decision-making process aiming at a better FCC implementation. The benefits of this model are clear. However some factors and indicators must be taken into account before implementation, especially those concerning stress generation on professionals.

Early mobilisation

It is well known that survivors of critical care suffer physical and psychological morbidities to deal with. A post-intensive care syndrome can be identified in children including neurocognitive and psychological morbidity (Herrup et al. 2017). Early mobilisation (EM) is one of the actions that can be done to mitigate it. Historically, children in the PICU were profoundly sedated and immobilised. In regards to this issue, there is currently an ongoing transformation promoted by the ICU Liberation. This is a movement that advocates for mobility in terms of allowing critically ill patients to be as safely awake, interactive, and mobile as possible. An ABCDEF bundle is used to achieve this objective (Ely 2017) (**Table 2**). In adults, it is shown how EM is feasible, safe, improves functional outcomes and increases patient satisfaction (Schweickert et al. 2009; Burtin et al. 2009). Wieckzorek et al. (2016) published their experience with the quality improvement project, PICU Up! This project consists of stratified rehabilitation levels based on the patient's clinical status ranging from passive range of motion activities to ambulation. PICU Up! is an inspiring project that has encouraged other units to advance in this field. However, we should keep in mind that this project requires a multidisciplinary approach (therapists, physicians, nurses, ancillary staff from child life, and family). The most common barriers to EM in children are the lack of physiotherapy resources, and the concerns about safety. Despite these barriers, EM is beneficial, and each unit has to design their own project according to their resources. In upcoming years we will be faced with required improvements in this area.

Facing death in the PICU: implications for families and professionals

The objective of critical care is to provide support and cure to patients. Despite a low mortality rate in PICU, the manner in which professionals face and deal with this event remains a concern. The death of a child never is experienced as "natural" as it can occur in the adult population, especially in the elderly. Even when death is "expected," this experience is devastating for parents and stressful for professionals. Initiating palliative care treatment in the PICU confronts specific challenges that require a good understanding between families and health professionals, especially in regards to providing adequate care for a death with dignity. Thus, the need for a multidisciplinary approach and emotional support emerges as a compelling and essential requirement in these cases.

> "the newest treatments and the novel support therapies are indicators of the advancement achieved and have also become an encouraging stimuli for us to pursue our mission of paediatric care"

When necessary, religious rites and rituals for parents and family members have to be taken into account in the PICU in order to offer comfort. Communication skills are crucial to help families in this painful moment. Concerning professionals, child care in the PICU can disrupt their psychological balance, and moral distress can also be experienced in circumstances in which the practice is not performed aligned to their sense of duty. Previous structured talks with parents will play an important role in regards to this aspect (Garros et al. 2015). We encourage institutions to provide emotional support to professionals.

Safety in the PICU

Safety in the PICU is a real concern and a major priority for institutions. The diversity of treatments and techniques over the patients make them especially vulnerable to error. In addition, children require a complex pharmacological prescription because of their body weight and this fact adds new possibilities for error.

Actions focused on minimising error and

enhancing a climate of safety culture are required. The presence of a clinical pharmacist in the PICU clearly minimises medication errors (Maaskant et al. 2017). Simulation programmes in the PICU are effective both for training and error prevention (Fehr et al. 2017; di Nardo et al. 2018). This strategy should be complemented with mandatory leadership and teamwork specific for safety in the PICU.

Conclusions

Modern PICUs are at the cutting edge in technology and science applied to children's care. Professionals have to be continuously trained, and it is capital that institutions provide the means and resources for them to update their skills.

Smart PICUs and big data analysis applied to them will be the next frontier to be crossed in terms of challenging patients' perception on the upcoming personalised medicine model. The newest treatments and the novel support therapies are indicators of the advancement achieved and have also become an encouraging stimuli for us to pursue our mission of paediatric care.

In spite of all the breakthroughs in medicine, some old concerns cannot be dismissed. The well-being of children, families, and professionals must be highlighted as the core of our practice. Transforming a previously hostile environment into a comforting place where to take care of children is one of the most outstanding actions we can offer in the humanisation process of the PICUs. The curative power of a kind word with the best medical assistance, in a context of safety, represents the excellence that all children deserve and society expects. ■

References

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

Abbreviations

AAP	American Association of Pediatrics
CART	Chimeric Antigen Receptor
ECMO	Extracorporeal Membrane Oxygenation
EM	Early Mobilisation
FCC	Family-centred Care
ICU	Intensive Care Unit
PCR	Polymerase Chain Reaction
PICU	Paediatric Intensive Care Unit

Key points

- Acute medical conditions such as infections, respiratory diseases, injuries, and high complexity surgeries are the most common reasons for admission in the PICU.
- Admission into a PICU causes psychological distress for the patients and their families because of the emotional intensity they experience. A family-centred model is essential to provide the best care for children.
- Smart PICUs using Big Data predictive analysis including intelligent infusion systems will reduce administration errors and facilitate decision making.
- ICU Liberation is a movement that advocates for mobility in terms of allowing critically ill patients to be as safely awake, interactive, and mobile as possible.
- The curative power of a kind word with the best medical assistance, in a context of safety, represents the excellence that all children deserve and society expects.

Marcelo Malakooti
Medical Director
Lefkofsky Pediatric Intensive Care Unit
Director, Innovation/Strategy – IGNITE Innovation
Ann & Robert H. Lurie Children's Hospital of Chicago
Assistant Professor, Division of Critical Care Medicine
Northwestern University, Feinberg School of Medicine

@innovatedoc

MMalakooti@luriechildrens.org

Virtual reality experience in the PICU

A pilot study at the Ann & Robert H. Lurie Children's Hospital of Chicago

An overview of the virtual reality programme at the Ann & Robert H. Lurie Children's Hospital of Chicago and its potential benefits on patient outcomes.

Ann & Robert H. Lurie Children's Hospital of Chicago has introduced virtual reality into their paediatric intensive care unit. A pilot study was conducted with 32 participants between the ages of 3 and 17 years to evaluate whether the stimulation and interaction that virtual reality offers will mitigate the risk of delirium and other cognitive and emotional impairments as well as improve outcomes for these children (Badke et al. 2019).

The primary goal of the virtual reality programme was to create an "outlet" for patients in the Paediatric Intensive Care Unit (PICU) who, like many hospitalised patients, are usually confined to the four walls of their hospital room. While there are ways to engage and offer enjoyable, growth-oriented experiences for these patients who are receiving the highest level of medical support, patients often spend much of their days watching TV or movies, which are non-interactive and one-dimensional. We wanted to bring the outside in, and simulate high-stimulus experiences for our recovering critically ill patients. Virtual reality (VR), being immersive in nature, was one way we were hoping to achieve this. Essentially, we used a disposable VR headset, in order to avoid cross-contamination between patients, and provided a smartphone that displayed VR, 360-degree videos we curated by age and experience preferences. In the study, patients were given a time limit of exposure, and patient and caregiver responses were recorded.

Why a virtual reality programme?

We know that critical illness, and importantly the recovery period, can in itself present complications for the patient, including delirium, weakness, and susceptibility to immune dysregulation. Critically ill adult patients have shown a positive response to being exposed to nature and other interactive stimuli, in an effort to combat co-morbidities. Critically ill children at all developmental levels can also benefit from interactive experiences that provide positive stimulation that otherwise are absent from the ICU environment. This programme complements the partnership that our PICU has with Child Life Specialists and Creative Arts Therapists. It is an immersive, 360-degree visual experience that offers an opportunity for patients to be active in choosing experiences that improve their sense of well-being. For this study, we were

Image Credit: Ann & Robert H. Lurie Children's Hospital of Chicago

The IGNITE Innovation Program


Virtual reality in the PICU

Image Credit: iStock

largely general with providing the experience to a wide array of patient conditions, although those who have a prolonged hospitalisation may benefit the most.

Benefits of the programme

For this study, we wanted to evaluate feasibility, satisfaction with the experience, and overall enjoyment. It was important for us to also include the parents' perceptions of their child's reaction, as they had the most exposure to their child throughout their hospitalisation and would hopefully be able to notice a difference. We found that the majority of patients and their parents thought that VR was easy to use, had minimal adverse effects, was enjoyable, and that they would want to continue using VR throughout their hospitalisation.

We are in the process of studying a number of clinical parameters for those patients exposed to VR, to understand if there is a measurable effect on some of these health indicators. Aside from the clinical implications, we will be offering the platform to patients as a distraction tool in the interim.

In this feasibility study, we were limited in what we could conclude about the short- and long-term psychological benefits of VR. However, with the help of Dr. Bonnie Essner, a psychologist and one of our co-authors, this is another outcome that our team will be studying. There is growing evidence that daily doses of enjoyable moments can have a big impact on children's interpretation about their safety and well-being, and in turn, can protect against psychological comorbidities. We'd like to better understand the role of VR in children's in-hospital and longer-term adjustment as they recover from critical illness.

> **"critically ill children at all developmental levels can benefit from interactive experiences that provide positive stimulation that otherwise are absent from the ICU environment"**

We are in the process of studying outcomes in addition to a number of other parameters to better understand what clinical impact VR may have on patients in our PICU, and we are excited to share these results.

Parents' response to the virtual reality programme

We surveyed all parents who observed their child experiencing the VR, and the majority reported that they enjoyed watching their child during the session, that it had a positive impact on their child's mood, and that they would want to repeat the experience. We even had some parents report, quite emotionally, that it was the happiest they had seen their child in some time.

Future prospects

We are currently studying the clinical impacts of VR on a larger patient population, and in different clinical uses cases, in addition to better understanding its impact on mood. Our plan is to widely implement this as an additional tool that can be offered to patients in the PICU.

Identifying and creating novel uses for existing, or even new, technology in ways we have not considered before is the cornerstone of multi-disciplinary innovation in our PICU. Not only can this provide a substantial positive impact on our patients, but it also continues to introduce alternative methods for recovery for these patients. We hope to continue to expand on this, and similar programmes, in offering our patients and families holistic, well-rounded care. ■

Key points

- Ann & Robert H. Lurie Children's Hospital of Chicago has introduced virtual reality into their paediatric intensive care unit.
- Critically ill children can benefit from interactive experiences that provide positive stimulation.
- The majority of patients and their parents thought that VR was easy to use, had minimal adverse effects, was enjoyable, and that they would want to continue using VR throughout their hospitalisation.

References

Badke C, Essner B, O'Connell M, Malakooti M (2019) An Innovative Virtual Reality Experience in the PICU: A Pilot Study. Pediatric Critical Care Medicine.

Theodoros Kyprianou
Assoc. Professor of Medicine
Medical School University of Nicosia (UNIC)

Academic Lead in Critical Care Anaesthesia and Emergency Medicine SGUL/UNIC MBBS-4

Academic Board/Co-coordinator MSc Applied Health Informatics & Telemedicine
Open University of Cyprus

SC1 (Health) EU HORIZON 2020 Program Committee Member-Expert/Brussels

kyprianou.t@unic.ac.cy

cy.linkedin.com/in/theodoroskyprianou

Seven steps to design, procure, implement and maintain a Clinical Information System for your intensive care unit

How to design, procure, test, parameterise, implement and maintain a Clinical Information System for an intensive care unit.

Introduction:

e-Health applications, in our case Clinical Information Systems (CIS) or Patient Data Management Systems (PDMS), are taking medicine by storm, and intensive care is not an exception. Ensuring delivery of safe, cost-effective, high-quality care in the most expensive hospital beds, has been the major underpinning. Countries with higher GDP tend to have most installations, penetration being less in smaller, poorer countries. The impact of CIS use on patients' outcome (Prgomet et al. 2017), LOS (Levesque et al. 2015) and hospital costs has been examined and somewhat documented in several studies, though a recent meta-analysis (Thompson et al. 2015) disputed the evidence, admittedly not yet enough to support firm, generalisable conclusions. Several factors may contribute to this variability: the complex nature of multiple processes of ICU care a CIS aims to organise, different ICU population and case mix, lack of standardisation of CIS minimum functionality and usability specifications, the inherent difficulty to comparatively assess users' compliance, etc.

To design, procure, test, parameterise, implement and maintain a Clinical Information System for an intensive care unit is a quite complicated project. It not only requires a sizable budget (probably 25.000 – 60.000 K Euros/bed, depending on the country and specifications), but it involves substantial managerial and leadership skills as well as wide -eventually- "bottom-up" acceptance and users' active adoption. Most importantly, it constitutes a substantial change in the way the team delivers care, though at the same time the system should be "adapted" and "customised" to fit local health-care professionals' and patients' needs. This fine balance to be kept is not trivial and should be reflected in the outline of specifications as well as the parametrisation and implementation plan. CIS/PDMS is not another equipment piece to buy. It is a project with an open-end life cycle that is to be designed, implemented and maintained with constant improvement/parameterisation. We have deliberately left cybersecurity issues and GDPR compliance as well as IPRs out of the scope of this article as we will come back soon with a practical guide on how to deal with these important issues.

> "clinical Information System for an intensive care unit should be adapted and customised to fit local health-care professionals' and patients' needs"

Below we describe 7 essential steps towards this direction:

STEP 1: Define the project extension – Local? Cluster ICUs? ICU purposed solution OR part of a Hospital Information System (HIS)?

The decision to procure the installation of a CIS/PDMS in an ICU in a hospital either refers to an isolated installation or might include other/all ICUs of the same hospital, or even ICUs in other hospitals residing in the same area or other areas in the country. The decision is often beyond the reach of clinicians -even of senior clinicians- as it may bear political and economic dimensions that are part of or might affect general governmental/regional health authorities' policies. In the case of more than one installation within the same tender, measures should be taken, and mechanisms should be set in order to involve all clinical teams in the decision-making process, accommodating their concerns and needs to the extent possible. In either case, structured interaction between ICUs within the same hospital/different hospitals is strongly encouraged and the technological solutions to facilitate such interactions exist in the market and should be incorporated

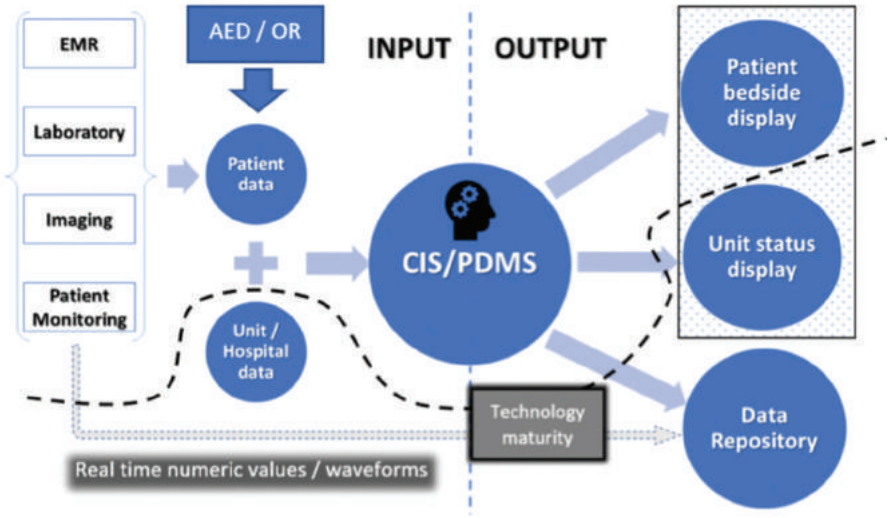


Figure 1: A graphical representation of data input & output for a CIS

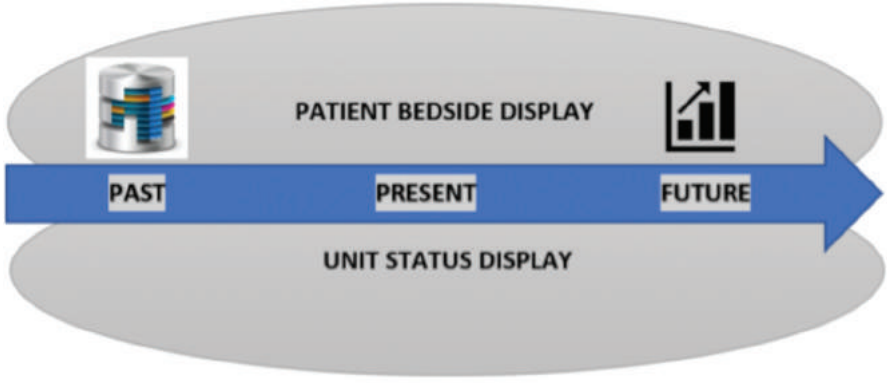


Figure 2: CIS display dimensions: patient vs. the unit, past (collection) vs. present (projection) vs. future (prediction)

into the product specifications, even if the ICUs involved have different CIS/PDMS vendors. Despite being in the context of this interaction, ICU tele-medicine systems are beyond the scope of this article and shall be offered in one of the next issues of ICU Management & Practice.

In another note, ICU purposed CIS/PDMS are now increasingly being substituted with modules of more generic Hospital Information Systems, claiming better integration, interoperability and cost control. This trend fired serious controversy since it frequently doesn't engage users from ICUs in a meaningful way and customisation process has been poor that ends to poor usability, an inherent problem of those systems (von Dincklage et al. 2017). On the other hand, we must admit, the arguments for an all-encompassing, integrated HIS are quite solid. An ICU senior practitioner who is asked her/his opinion should be very clear in terms of the required functionality but, in my opinion, should not fanatically insist to either option beforehand as what really matters is what is offered.

STEP 2: Explore initial "perceived" needs to formulate the outline of specifications - think big - include personnel/patients from the beginning and at all stages

When it comes to IT solutions, our generation's perceived needs are poorly correlated with the capabilities of even commercially available systems. If right from the beginning the clinical team "undermines" its position by expressing minimal functionality requirements then the game will be gradually lost as the vendor will neither have the motivation to offer more functionality in a certain price range, nor will deploy the resources necessary to offer it. It is thus, of paramount importance to include the younger, "native" to the "technology land" generation, to the decision-making process, especially clinical routines re-design and specifications outline. We should rather think big, and we might subsequently downsize the required functionality and modify the specifications accordingly, as a function of cost and (careful, real!) technology restrictions. All companies have pre-set questionnaires to record pre-installation functionality and clinical routines as well as users' demands and maturity in handling complex IT systems. An ICU team might want to give its own questionnaire based on local needs and philosophy of care. It is also very important to visit an installation site to discuss with fellow clinicians, nurses and AHPs regarding their experience, strengths, and weaknesses of the system installed.

Figure 1 and **Figure 2** graphically display the basic functionality of a CIS in terms of data input, data output and the time dimension. **Figure 1** - INPUT: Interface with patient's monitoring systems (multi-parameter monitor, stand-alone monitors), ABG/POC testing devices and main therapeutic & organ support systems (ventilator, haemofiltration, ECMO etc), patient's EHR, LIS (laboratories) and PACS (imaging, including POC US studies to be downloaded to PACS and accessed thereafter) as well as any OR/AED electronic records is considered as standard and should be included to the outline of specifications. OUTPUT: should include a health professional display with patient data visualised in numerical and graphical means and in an intuitive order to facilitate, spot diagnosis, decision making and follow up. Unit status panel should be provided for ICU management and should serve as a live report on the main statistics and important events/figures pertaining to ICU function, i.e. trends in mortality, morbidity, complications, organ failure, LOS, ventilator days, procedures, tech/other resources use per bed/area/ICU, etc. This could be provided by CIS/PDMS itself or data could be fed/processed in another programme, depending on local needs. The bottom-line is to allow for a meaningful and timely

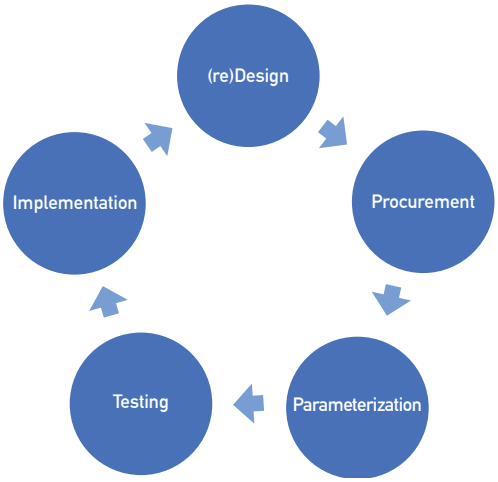


Figure 3: The CIS life cycle

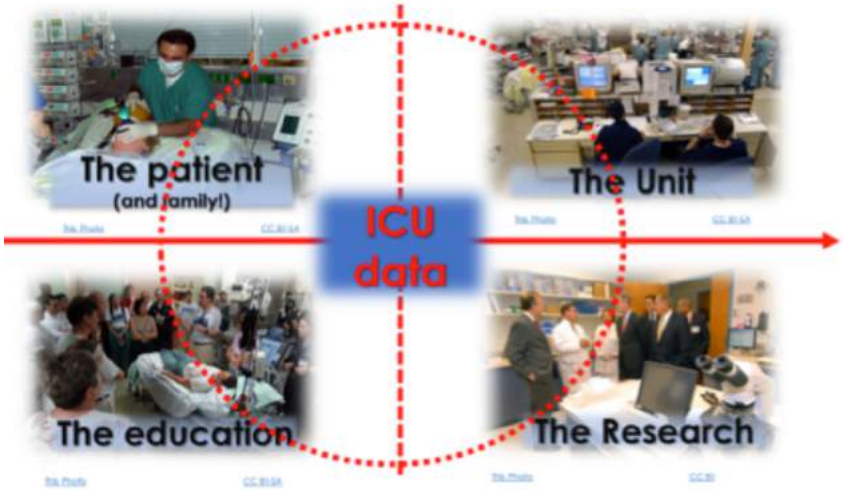


Figure 4: ICU vertical ecosystem cycle, based on data collection, projection and prediction

update of ICU management team regarding unfavourable/dangerous trends or isolated incidents. Including patients' group(s) into the process might prove beneficial as it offers the added value of creating a "community" beyond users and administrators which could protect the process and extend its life-cycle.

STEP 3: Bring in expertise, set up an interdisciplinary team (IDT) (not MDT!) and create a community of "champions" & "super users"

An ICU (or hospital/healthcare authority) based interdisciplinary project governance team having regular (preferably open) meetings with publicly available agenda and minutes with action points and timelines is essential to allow for effective procurement. The presence and/or the structured input of physicians, nurses, physiotherapists/RTs, clinical dieticians, clinical pharmacists, health/clinical psychologists, health managers, etc should be sought. The coordinator/project manager should ensure meaningful interaction between them as the transition to a "multi-disciplinary" team is not favourable as it involves fragmentation of the processes and loss of global view and integrated approach. We would like to emphasise the role of an experienced health psychologist in the process as she/he would be able to identify important barriers to adoption and implementation of the system beforehand. This, in turn, could be translated into an action plan to include Ftf/group discussions, workshops, etc to overcome the barriers identified.

> **"ideally, a CIS should have 2-4 health professionals from the champions team (highly skilled and dedicated) who shall share a full-time equivalent system administrator role"**

ICU professionals who are particularly skilled and oriented in IT applications could be proposed to participate more actively in the process of writing specifications, tendering, installing and operating the system, but mainly in facilitating implementation longitudinally by helping and encouraging their colleagues as well as safeguarding the system from misuse. Ideally, a CIS should have 2-4 health-professionals from the champions team (highly skilled and dedicated) who shall share a full-time equivalent system administrator role, particularly in the case of larger units with high patient turnover. The champions and super users will become invaluable when it comes to the implementation of early warning systems, a feature which requires mature users' community to be implemented successfully and sustainably. The idea is to "infiltrate"- ideally - all shifts with one or two health professionals from the aforementioned group in order to cover 24/7.

STEP 4: Secure budget/cash flow and choose tender method

Securing funding necessary to conclude procurement, installation and ongoing, meaningful support is of crucial importance as this kind of project can easily "die" if procurement lasts for a long period of time. We should be reminded that this installation is usually composed by a conglomeration of software whose life cycle becomes progressively smaller. Additionally, the window of opportunity in relation to other installations in the hospital/area is usually narrow. Tendering method is usually determined by hospital/health authorities of the region or the central government. It is, however, of paramount importance for us - the healthcare professionals - to ensure that the tender process: a) incorporates qualitative assessment criteria and not only cost-related criteria; b) involves exhaustive testing of the proposed solution in demo conditions and – ideally - visiting an installation site before contract is signed; c) includes explicit clauses regarding downtime, emergency situations management etc; d) goes into detailed description of data presentation screens, analysis, reports

and other services and products provided as devil is in the details; e) price for extra services, parameterisation, etc is provided in a way that costs could be pre-calculated and budgeted without major deviations, ideally from the beginning. Of course, use of the system will largely define the needs, but, a modular installation is always a solution in case the budget is not enough for an all-encompassing solution in the beginning.

Tender methodologies that allow hospital authorities to negotiate with vendors in a preliminary stage and competitively develop specifications are the most attractive when there is budget available for software/services developments beyond the commercially available solution package. It is, however, a time-consuming process, most suitable for larger establishments with many types of ICUs and complex needs.

STEP 5: Design a realistic project management plan (PMP)

Setting up a PMP is not a trivial task, and in the case of big installations, particularly at the hospital or health authority region level, a full-time professional project manager is required from the beginning and through all steps described here. This plan should be negotiated with all stakeholders in order to consider potentially conflicting (but also synergistic) activities pertaining to other ICUs/departments/hospitals as well as to ensure adequate staffing levels to allow for the extended periods of personnel training. Timelines and bilateral interdependencies of every phase of the project should be carefully considered, especially when interdependencies could potentially affect critical hospital processes like bidirectional patients' flow towards and from operation theatres and A&E. In case a professional project manager is not available to coordinate the project and a health professional is to undertake this responsibility, handy project management manuals (telemedicine-momentum.eu/) and open-source/commercial software might be of help.

STEP 6: Set and follow up performance and outcome indices - usability

Setting performance indices and a system to follow them up, troubleshoot accordingly and inform the project/unit management and the IDT meetings, is of paramount importance as it allows for early interventions that can maximise success. Such indices may entail the functionality and failures of the system in general (hardware and software) as well as specific modules, the intra/inter-hospital interoperability of the system, the personnel behavior, patterns of use of the system (including time required for certain functions), inaccuracies and mistakes, misuse, etc. CIS "usability" (Lee et al. 2018) has been a major topic of dispute between the users' community and the industry in the last years. Consequently, it sounds prudent to survey and record usability issues in an organised format. When observations lead to a robust and mature case, this should be moderated with the vendor either adapting the software functionality or adapting the non-clinical routine or both. When it comes to problems in serving clinical routines, customisation should be the primary responsibility of the vendor, and this should have been regulated in specs (see STEP 2 above). Clinical performance - outcome (ICU/hospital mortality, morbidity, complications, length-of-stay, ventilator-free days, sedation-free days, etc) is, of course, the holy grail of healthcare technology effectiveness. CIS gives a unique opportunity to follow these indices systematically.

STEP 7: Creating a life cycle for your CIS to serve the ICU "vertical" ecosystem

Following the STEPS described above (1-6) a life cycle (**Figure 3**) is created for the CIS rendered sustainable if and only if the community that lives in continues to follow a structured and timed sequence of (re)design, procurement, parameterisation, testing, and implementation. Let's now zoom out to a bigger picture. Each ICU in the digital era grows its own ecosystem of IT applications serving diverse functions (clinical routine, education, and research) and stakeholders (healthcare professionals, patients/families, administrators) as it is schematically shown in **Figure 4**. CIS will not necessarily and directly serve all those needs; however, it should serve as a data hub that will enable these applications. We identify this ecosystem as "vertical" juxtaposed to the "horizontal" ecosystem that refers to the hospital and regional/national e-Health applications network. It is thus, of fundamental importance to foster interoperability at all levels. ■

Key points

- Implementing and maintaining a Clinical Information System for an intensive care unit is a quite complicated project that requires a sizable budget, substantial managerial and leadership skills and a bottom-up acceptance and users' active adoption.
- An effective CIS system requires structured interaction between ICUs within the same hospital/different hospitals.
- It is of paramount importance to include the younger, "native" to the "technology land" generation, to the decision-making process, especially clinical routines re-design and specifications outline.
- The presence and/or the structured input of physicians, nurses, physiotherapists/RTs, clinical dieticians, clinical pharmacists, health/clinical psychologists, health managers, etc should be sought.
- Securing funding necessary to conclude procurement, installation and ongoing, meaningful support is of crucial importance.
- A full-time professional project manager is required from the beginning and through all steps described.
- Setting performance indices and a system to follow them up, troubleshoot accordingly and inform the project/unit management and the IDT meetings, is also very important.
- It is of fundamental importance to foster interoperability at all levels.

References

Lee Y, Jung M, Shin GW, Bahn S, Park T, Cho I, Lee J (2018) Safety and Usability Guidelines of Clinical Information Systems Integrating Clinical Workflow: A Systematic Review. Healthcare Inform Res, 24(3):157-169.

Levesque E, Hoti E, Azoulay D, Ichai P, Samuel D, Saliba F (2015) The implementation of an Intensive Care Information System allows shortening the ICU length of stay. J Clin Monit Comput, 29(2):263-9.

PRINCE2 or Agile for more complicated projects. Scrum or Kanban for less complicated projects. Avaialble from telemedicine-momentum.eu/

Prgomet M, Li L, Niazkhani Z, Georgiou A, Westbrook JI (2017) Impact of commercial computerized provider order entry (CPOE) and clinical decision support systems (CDSSs) on medication errors, length of stay, and mortality in intensive care units: a systematic review and meta-analysis. Journal of the American Medical Informatics Association, 24(2):413–422.

Thompson G, O'Horo JC, Pickering BW, Herasevich V (2015) Impact of the Electronic Medical Record on Mortality, Length of Stay, and Cost in the Hospital and ICU: A Systematic Review and Meta-analysis. Crit Care Med, 43(6):1276-82.

von Dincklage F et al (2017) Investigation of the Usability of Computerized Critical Care Information Systems in Germany. Journal of Intensive Care Medicine.

Respiratory physiotherapy in critically ill patients

Respiratory pathologies are among the most common causes of admission to critical care. Respiratory physiotherapy represents a fundamental part of the standard practice in ICU. The following review provides a practical and feasible description of the main physiotherapeutic tools and strategies that can be applied to critically ill patients.

Vittoria Comellini
Respiratory and Critical Care Unit
University Hospital St. Orsola-Malpighi
Bologna, Italy

vittoria.comellini@libero.it

Stefano Nava
Department of Specialistic Diagnostic and Experimental Medicine (DIMES)
Alma Mater Studiorum
University of Bologna
Bologna, Italy

stefanava@gmail.com

Antonio Artigas
Critical Care Center
Sabadell Hospital
University Institute Parc Taulí
Autonomous University of Barcelona
Ciberes, Spain

aartigas@clinic.cat.

Introduction

Respiratory physiotherapy [RP] is an integral part of the multidisciplinary approach to patients hospitalised in intensive care units [ICUs] (Gosselink et al. 2008).

The survival rate of patients with life-threatening conditions who are admitted to an ICU has significantly increased through improvements in medical care. Unfortunately, for those who do survive, nearly half present long-term impairments in physical, cognitive and/or mental health, often due to post-intensive care syndrome [PICS] (Needham et al. 2012) and weakness acquired post-ICU, regardless of the diagnosis of admission to the ICU (Ohtake et al. 2018; Kamdar et al. 2017; Dinglas et al. 2017). Critical illness is frequently associated with long-term bed rest and inactivity, and it may lead to ICU-acquired muscle weakness [ICUAW] (Stevens et al. 2007), and other deleterious effects (Cirio et al. 2003), which in turn are strongly associated with increased morbidity, physical impairments and mortality, both at short and long-term (Herridge et al. 2011; Hermans et al. 2014; Unroe et al. 2010; Pandharipande et al. 2013). It has been recognised that physical and psychological recovery after a period of critical illness is slow and often incomplete (Wilson et al. 2018) and in certain conditions, it leads to a cognitive impairment comparable with Alzheimer's disease, especially in older patients (Pandharipande et al. 2013), and this decreases quality of life, for up to 5 years after their original illness (Heyland et al. 2005; Herridge et al. 2013; Iwashyna et al. 2010; Herridge et al. 2016a; Fan et al. 2014; Cox et al. 2009; Herridge et al. 2016b; Barnato et al. 2011; Turnbull et al. 2016; Chan et al. 2016; Kamdar et al. 2017).

Limiting the period of immobility and promoting early physiotherapy enhance recovery and influence or even prevent physical impairments and poor outcomes (Fuke et al. 2018; Schweickert et al. 2009; Schaller et al. 2016; Bourdin et al. 2010; Kayambu et al. 2013; Stiller et al. 2013). The aims of early physiotherapy consist in improving patient's quality of life and preventing ICU-associated complications like deconditioning, ventilator dependency, and respiratory conditions. In addition, early rehabilitation can be extended beyond physical therapy to include cognitive therapy (Brummel et al. 2014).

Since respiratory pathologies are among the most common causes of admission to critical care, RP represents a fundamental part of the standard practice in ICU (Vincent et al. 2002; Berney et al. 2012). Respiratory physiotherapists provide various types of care, from acute respiratory interventions to rehabilitation. They treat both intubated and spontaneously breathing patients, and their key roles include management of respiratory, but also neurological and musculoskeletal complications (Pathmanathan et al. 2015).

The European Respiratory Society and European Society of Intensive Care Medicine Task Force on Physiotherapy for Critically Ill Patients in 2008 identified targets for physiotherapy for intensive care patients and summarised the literature regarding the available effective physiotherapy interventions (Gosselink et al. 2008). The Society of Critical Care Medicine recommends a comprehensive treatment for ICU survivors during all phases of recovery (Elliott et al. 2014; Hanekom et al. 2011). The authors developed a clinical management algorithm for early physical activity and mobilisation of intensive care patients in order to decrease clinical variability and to improve patient safety. Recently Sommers et al. provided a statement that explains safety criteria for the early mobilisation of intensive care patients (Sommers et al. 2015).

The purpose of this review is to update the evidence base regarding the application of RP to adult critically ill patients, with the goal of supporting and implementing clinical daily practice. This review provides

Table 1. Contraindications to respiratory physiotherapy in ICU

Absolute contraindications	Relative contraindications
• Recent myocardial ischaemia • Heart rate <40 and >130 beats/min • Mean Arterial Pressure (MAP) < 60 mmHg and > 110 mmHg • High inotrope doses • Oxygen Saturation < 90% • Fractional concentration of inspired oxygen (FiO2 < 0.6) • Positive End Expiratory Pressure (PEEP): > 10 cm H2O • Respiratory Rate > 40 breath/min	• Decreased level of awareness/consciousness • Richmond Agitation Sedation Scale (RASS) score: -4, -5, 3, 4 • Sweating • Pain • Fatigue • Unstable fractures • Presence of lines that make mobilisation unsafe • Acute head injury or neurological instability: Intra Cranial Pressure (ICP) > 20 cmH2O • Undrained pneumothorax or Emphysematous bullae • Recent pulmonary surgery • Severe bronchospasm • Temperature > 38.5°C

a practical and feasible description of the main physiotherapeutic tools and strategies that can be applied to critically ill patients.

Method of systematic literature search

We performed a systematic computerised literature search of the electronic databases PubMed, Cochrane and Scopus for papers published in English in the last 20 years combining the following keywords and medical subject headings: intensive care, pulmonary rehabilitation, respiratory physiotherapy, critical illness, acquired weakness, early physiotherapy, and chest physiotherapy. No limitations in the search strategy were inserted, except for the exclusion of case reports, comments or letters.

Selection of patients to treat, monitoring and safety

Although several studies described the safety of early physiotherapy (Brummel et al. 2014; Schweickert et al. 2009; Morris et al. 2016), the application of techniques to critically ill patients is often difficult because of the critical respiratory conditions, necessitating medication and invasive equipment. Oftentimes these severe respiratory diseases are associated with haemodynamic compromise, and this limits the possibilities for applying the physiotherapy interventions even more. In addition, the medical situation of these critically ill patients can rapidly change. Therefore monitoring patients' clinical status before and during physiotherapy sessions is of pivotal importance, first of all for patients' safety. Changes in vital parameters (blood pressure, heart rate, saturation of peripheral oxygen, respiratory rate, dyspnoea) should be monitored during each treatment session, and in case of deterioration, the intervention should be stopped. However, adverse events are generally rare during RP (Zeppos et al. 2007; Bailey et al. 2007), with the most common ones represented by decreases in oxygen saturation, changes in mean arterial pressure (both increase and decrease), and arrhythmias. Risk factors for these adverse events are haemodynamic instability, presence of cardiac comorbidities and abnormalities of vital signs before intervention.

> **"limiting the period of immobility and promoting early physiotherapy enhance recovery and influence physical impairments and poor outcomes"**

In order to increase the safety of RP, as part of the clinical reasoning process, every patient should be screened for the presence of absolute and relative contraindications, considering potential risks and benefits of each treatment. During this decision process, collaboration between all the members of the intensive care multidisciplinary team (intensivist, physiotherapist, nurse) is essential. The main contraindications to RP are shown in **Table 1**.

For every patient, we recommend assessment of global mental functions, responsiveness and consciousness and ability to cooperate. It should be noted that a significant reduction in vigilance, up to coma, does not represent an absolute contraindication to RP, because even in patients with low RASS score it's possible to apply passive techniques. Other aspects to be evaluated are range of joint motion, muscle strength, and tone, sensory function, functional ability [e.g. transfers in and out of the bed, standing balance and walking] (Parry et al. 2017). In conscious patients, it's important to monitor exertion during exercise (six-minute walk test, Borg score). All these parameters can be used to evaluate the impairments of every single patient and to programme tailored interventions.

Probably the biggest problems that clinicians have to face during RP are represented by barriers like staff and patient's safety concerns, perceived workload, general lack of confidence that rehabilitation may improve outcomes, and lastly lack of updated guidelines.

Respiratory physiotherapy interventions

The RP interventions that are recommended for critically ill patients hospitalised in the ICU are presented in **Table 2**. For clinical practice, we divided the recommended physiotherapy interventions into two groups; interventions for patients who are able (active interventions) and interventions for those who are not able (passive interventions) to follow instructions, determined primarily by the level of consciousness.

The main goal of RP is minimising the adverse effects of critical illness and intubation on the respiratory system (Goligher et al. 2019), restoring respiratory and physical independence, preventing the need for subsequent dependence on mechanical ventilation and subsequent hospitalisations and improving patient's quality of life. First of all this is achieved by the reduction of patient's dependency on the ventilator, reduction of secretion retention, atelectasis and pneumonia, maintenance or recruitment of lung

Table 2. Respiratory physiotherapy interventions.

Active interventions	Passive interventions
• Hyperinflation (Deep breathing exercises, incentive spirometry) • Drainage of endobronchial secretions • Hydration and airway humidification • Suctioning • Mechanical insufflation-exsufflation • Manual techniques (postural drainage, percussion, vibrations) • High-frequency oscillations (IPV, HFCWO) • Positive expiratory pressure (PEP) • NIV • Positioning • Mobilisation • Respiratory muscle training (RMT)	• Hyperinflation (manual or with ventilator) • Recruitment manoeuvres • Drainage of endobronchial secretions • Hydration and airway humidification • Suctioning • Mechanical insufflation-exsufflation • High-frequency oscillations (IPV, HFCWO) • Positioning • Mobilisation • Passive Exercise • Electromuscular stimulation (EMS)

volume, improvement of regional or global ventilation and compliance, improvement of ventilation/perfusion match, reduction of airway resistance and work of breathing, and optimisation of oxygenation. Not of less importance are the preservation and improvement of respiratory and peripheral muscle strength. Finally, an ICU early rehabilitation programme can generate net financial savings for the hospital, as shown by the financial model established by Lord et al. on actual experience and published data (Lord et al. 2013).

In the following section, we will discuss briefly the main interventions, dividing them into four major categories: techniques for lung hyperinflation, drainage of endobronchial secretions, mobilisation and muscular training.

1. Lung hyperinflation

Patients admitted to ICUs and affected by a respiratory disease frequently incur alterations of lung volumes, atelectasis, and reduction of respiratory flows that leads to increased pulmonary shunt, and impairment of gas exchange. All these detrimental effects are more pronounced in the case of mechanically ventilated patients.

Lung hyperinflation has been recognised as an important aspect to prevent atelectasis and to achieve recruitment of areas of pulmonary collapse leading to improved lung compliance and gas exchange (Stiller 2000). Moreover, it increases the movement of pulmonary secretions toward the central airways (Denehy 1999). This chest physiotherapy technique can be applied manually or through a ventilator.

Manual hyperinflation (MHI) involves the delivery via a manual resuscitator bag of transient tidal volumes larger than baseline (Hodgson et al. 1999); the delivery of a slow inspiration is usually followed by a 2–3 seconds inspiratory hold, and a fast, uninterrupted expiratory flow. MHI is commonly applied in patients under mechanical ventilation (MV), but this involves disconnecting the patient from the ventilator. It may stimulate cough and move the airway secretions toward the larger airways, from where they can be easily suctioned. MHI can prevent airway plugging and pulmonary collapse, and improve oxygenation and lung compliance (Paulus et al. 2011). There are different MHI bags available; some of them have PEEP valves within the circuit to ensure patients maintain PEEP and reduce de-recruitment and atelectotrauma. This is particularly useful in patients who are PEEP-dependent, such as patients with acute respiratory distress syndrome (ARDS). MHI can be performed using 100% oxygen, air alone, or a mixture of both. It is widely recognised that patients anaesthetised and ventilated on 100% oxygen can develop lung atelectasis; however, if hyperinflation is performed with an airway pressure of 40 cm H_2O and the pressure is maintained for a number of seconds, any atelectasis that has occurred is re-expanded.

The possible physiological side effects of delivered air volume, flow rates, and airway pressure must be carefully considered (Paulus et al. 2012). The most common short term and probably non-relevant side effects are reduction in cardiac output, alteration of heart rate and increase of central venous pressure.

Hyperinflation breaths can also be delivered while the patient is on ventilation. In spontaneously breathing patients **ventilator hyperinflation (VHI)** is achieved by applying incremental increases in pressure support or volume delivered during controlled ventilation, in order to reach a predetermined target volume. Usually, during the manoeuvre it's useful to reduce the respiratory rate as well as the inspiratory flow.

Only two studies (Berney and Denehy 2003; Clark et al.1999) have compared MHI and VHI: the techniques were found to be equally effective at clearing pulmonary secretions and improving static pulmonary compliance. Other authors demonstrated that lung hyperinflation reduces the incidence of nosocomial pneumonia in mechanically ventilated patients (Ntoumenopoulos et al. 2002). An advantage of VHI, as opposed to MHI, is less risk of de-recruitment and atelectotrauma. Indeed during VHI, it's possible to maintain a determined PEEP as the patient is not disconnected from the ventilator.

Recruitment maneuvers (RM) are similar in principle to VHI, and they are used more frequently by medical staff, especially to treat patients who have ARDS. They involve transient elevations in airway pressure applied during mechanical ventilation to open collapsed lung units and increase the number of alveoli participating in tidal ventilation. Because of significant clinical heterogeneity among different clinical trials, the effects of this treatment on clinical outcomes has not been well established. A recent meta-analysis has shown that a ventilation strategy that included RM in ARDS patients reduced ICU mortality without increasing the risk of barotrauma, but it had no effect on 28-day and hospital mortality (Hodgson et al. 2016). However, a recent RCT has disowned these results, showing that in patients with moderate to severe ARDS, a strategy with RM and titrated PEEP compared with low PEEP increased 28-day all-cause mortality (Cavalcanti 2017). In conclusion, nowadays the routine use of lung RM is not recommended.

When applying MHI, VHI, or eventually

and in selected cases RM, the clinician needs to be mindful regarding the possible adverse effects of these manoeuvres. The increase in intra-thoracic pressure and subsequent reduction in venous return may lead to a reduction in cardiac output and arterial pressure, compromising cardiovascular stability. The increase in tidal volume may also lead to volutrauma or damage to any recent surgical lung anastomosis. If there are concerns regarding the risk of barotrauma, a manometer can be put into the MHI circuit.

Deep breathing exercises, consisting of a sequence of deep breaths, using the diaphragm rather than accessory muscles of respiration can be an alternative for spontaneously breathing patients. Frequently this type of RP is performed with a device (incentive spirometry), that has the advantage of giving feedback on performance from the gauge. The use of such a device is not considered in the early phase of treatment, as these techniques require substantial co-operation from the patient.

2. Drainage of endobronchial secretions

Adequate and efficient clearance of endobronchial secretions is a crucial point for maintaining airway patency and reducing the number of infections, morbidity, and mortality of critically ill patients. Patients admitted to ICU often suffer from severe impairment of airway clearance capacity (Konrad et al. 1994). Muscular weakness reduces the strength and effectiveness of cough reflex, which in turn makes it more difficult to expel secretions. Moreover, in mechanically ventilated patients, it's added the impossibility of effectively closing the glottis due to the presence of the intratracheal tube in the proximal airway. Furthermore, the presence of a tracheal tube leads to bacterial translocation from the oropharynx to the lower airways.

Due to the combination of these factors, it's impossible to generate an expiratory flow sufficient for expulsion of the mucus. In turn retention of mucus represents a factor that determines the deterioration of respiratory conditions, creating a growth medium for bacteria leading to pneumonia and consequent prolongation of MV and length of stay, and increased morbidity and mortality (Sackner et al. 1975). Moreover, patients are often kept in semi-recumbent position in order to prevent aspiration phenomena and the consequent ventilator-associated pneumonia [VAP] (Salamone et al. 2016); however, in this position the trachea is oriented not horizontally but rather obliquely and the gravity force makes the function of mucociliary escalator diminished (Bassi et al. 2008). In addition, conditions such as prolonged entrapment, comorbidity, administration of drugs (especially sedatives, analgesics, and neuromuscular blockers), fluid restriction, and frequent respiratory infections contribute to the overproduction and accumulation of mucus (De Jonghe et al. 2007; Ray et al. 1974). Finally, MV is itself a cause of rapid deterioration of the diaphragm function, the main muscle involved in breathing, and therefore also in mucociliary clearance (Callahan 2008).

> **the main goal of RP is minimising the adverse effects of critical illness and intubation on the respiratory system**

As different mechanisms can be responsible for secretions retention, it's important for clinicians and physiotherapists to identify the problem correctly and select the correct intervention to facilitate sputum clearance. Different therapeutic strategies can be adopted to optimise bronchial hygiene and improve respiratory mechanics, including pharmacological and non-pharmacological treatments. It is unlikely to find a perfect system to clear the airway from the mucus. Generally, airway clearance regimes act through different mechanisms that improve airflow and reduce the viscosity of the mucus, both of which are important factors. Techniques usually exploit the gas-liquid interaction principle between the airflow generated by respiratory acts and the secretions contained within the airways (Benjamin et al. 1989). The mucus, pushed by traction forces generated by the aerial column that moves above it, moves deep into the airways (during the inspiration) or cranial direction (during exhalation). Part of the techniques for secretions drainage is based on the generation of an asymmetrical flow pattern, with an expiratory flow that exceeds the inspiratory flow, thus carrying the mucus outside the airways (Atkinson 2002).

In intubated and mechanically ventilated patients it is always advisable to ensure correct systemic **hydration** and appropriate airway **humidification** in order to prevent tenacity of the mucus and consequent adhesion and development of atelectasis. Correct humidification can be obtained via an active or passive humidifier. Contrarily, the routine use of N-Acetyl Cysteine or sodium chloride instillation are not recommended (Atkinson 2002).

In intubated patients with a tendency to retention of secretions, tracheo-bronchoaspiration often represents the terminal phase of the unblocking manoeuvres. When secretions are mobilised from the more peripheral airways centrally, they can be removed via suction. **Suctioning** can be performed through flexible bronchoscopy or using a catheter. In spontaneously breathing patients the catheter is usually inserted through the nostril, except in case of severe coagulopathy and basal skull fracture, when oro-pharyngeal airways is preferred. Vomiting and laryngospasm may occur if upper airway reflexes are still present. In patients with an artificial airway (endotracheal tube or tracheostomy), suction can be performed via an open or a closed technique. In hypoxaemic patients, suctioning may determine complications, particularly the deterioration of oxygenation and lung derecruitment, which have the potential to worsen lung injury. To prevent or limit these complications, an increased fraction of inspired oxygen (FiO2) should be administered or, when possible, open suctioning should be avoided, and closed systems should be preferentially used (Maggiore and Volpe 2011; Maggiore et al. 2013). Indeed the advantage of a closed circuit is that disruption of the circuit is minimised; however, no clear benefits have been demonstrated in terms of infection reduction.

Mechanical insufflation-exsufflation uses positive pressure to promote maximal lung

inflation through a gradual application of positive pressure, followed by a rapid switch to negative pressure. This change produces a high expiratory flow which simulates a powerful cough. The cough assist has proved to be effective in improving clearance in patients with neuromuscular diseases (Gomez-Merino and Bach 2002). Goncalves et al. found that the application of mechanical insufflation-exsufflation as part of an extubation protocol may reduce reintubation rates and ICU length of stay (Vianello et al. 2011; Goncalves et al. 2012; Guérin et al. 2011). Chatwin et al. compared conventional physiotherapy with physiotherapy plus in-exsufflation in patients treated with non-invasive ventilation (NIV); in-exsufflation shortened the treatment time in the ICU without any difference in secretion clearance (Chatwin and Simonds 2009). Despite these benefits, the use of this method is to be reserved only for selected cases among ICU-patients at high risk of severe hypoxaemia and development of atelectasis, since disconnection from the MV and application of negative pressure can aggravate the phenomena of airway collapse. Other main contraindications to this technique are undrained pneumothorax, major cardiovascular instability, and flail segments. Relative contraindications are emphysematous bullae and head-injury.

Postural drainage traditionally includes gravity-assisted positions, deep breathing exercises, chest clapping, shaking or vibration, and incentivised cough. Postural drainage is eventually associated with percussions, a technique that, when performed by a trained operator, has proved to be effective in facilitating the mobilisation of secretions. Percussions are performed using cupped hands to clap the chest wall over the affected part of the lung (Andrews et al. 2013). This combination of techniques was shown to improve lung collapse in mechanically ventilated patients (Chen et al. 2009). As an alternative to percussions, vibrations can be performed manually or using mechanical devices to compress with a high frequency the chest wall. McCarren and colleagues founded that vibrations increased peak expiratory flow rates by more than 50% over relaxed expiration (McCarren et al. 2006). Ntoumenopoulos et al. demonstrated a direct relationship between percussions and vibrations and the reduction in the incidence of VAP by 31% (Ntoumenopoulos et al. 2002).

High-frequency oscillations (HFOs) can be applied either directly to the airway opening (High-Frequency Ventilation, HFV; Intrapulmonary Percussive Ventilation, IPV), or to the surface of the rib cage (High-Frequency Chest Wall Oscillations, HFCWO, also called High-Frequency Chest Wall Compressions, HFCWC). The IPV consists of the application at the opening of the airways of high-frequency ventilation modality that can be superimposed on spontaneous breathing. Oscillations with a frequency typically between 10 and 20 Hz (Freitag et al. 2007) are generated by a compressor and transmitted inside the airway, inducing alveolar recruitment. IPV, therefore, creates a bias between expiratory and inspiratory flow, and in particular generates an expiratory flow that exceeds about 4 times the inspiratory flow. This may reduce respiratory muscle load and help to move airway secretions. A second mechanism through which IPV improves clearance is the modification of the rheological properties of mucus: there is evidence that the application of oscillations within the airways with a frequency between 12 and 22 Hz may decrease the viscosity and thickness of the mucus, thus favouring its mobilisation (Tomkiewicz et al. 1994). Positive effects from this technique have been shown in patients with respiratory distress, neuromuscular diseases, and pulmonary atelectasis (Chatburn 2007; Vargus et al. 2009: Dimassi et al. 2011).

> **different therapeutic strategies can be adopted to optimise bronchial hygiene and improve respiratory mechanics, including pharmacological and non-pharmacological treatments**

Physiologic effects of IPV were studied by Vargas et al. in intubated patients affected by chronic obstructive pulmonary disease [COPD] (Vargus et al. 2009). IPV promotes secretion clearance (Cioffi et al. 1989), gaseous exchange and it decreases the ICU stay in patients with COPD which undergo NIV (Antonaglia et al. 2006). Dimassi et al. assessed the short-term effects of IPV in patients at high risk for extubation failure who were receiving NIV after being extubated. This study concluded that both NIV and IPV reduced the respiratory rate and work of breathing (Dimassi et al. 2011). Studying a population of tracheostomised patients with prolonged weaning, Clini and colleagues documented that twice a day addition of IPV to regular treatment with conventional physiotherapy (CPT) improves gas exchange and expiratory muscle performance, reduces the incidence of nosocomial pneumonias, although it does not significantly reduce the number of atelectases and the need for toilet broncoscopies (Clini et al. 2006). Although some positive data have emerged about the possible benefits deriving from the use of IPV, to date the value of this method has not yet obtained consistent validations with regard to important long-term outcomes among patient requiring invasive mechanical ventilation (IMV). Therefore, IPV is recommended only for treatment atelectasis and retention of mucus in patients with COPD, cystic fibrosis or postoperative respiratory complications.

HFCWO is an airway clearance technique consisting in external chest wall oscillations applied to the surface of the chest using an inflatable vest that wraps around the chest. The high-frequency pulses and the consequent pressure fluctuations result in slight compressions and releases of the underlying thoracic surface. This produces an oscillatory air flow superimposed to the normal air flow presented by the patient in spontaneous breathing or to the air flow delivered by the ventilator in case of a patient on MV (Hansen and Warwick 1990). The effect of secretions mobilisation is determined through the development of a flow bias between inspiratory and expiratory flow, but also through the modification of the rheological properties of the mucus and the strengthening of the ciliary beating (King et al. 1983; Denton et al. 1968). HFCWO has a wide application among patients affected by cystic fibrosis and bronchiectasis or in

patients with neuromuscular disease, but only limited data are available on its use in the critical care settings. In a study conducted by Ndukwu et al. tracheostomised patients were more likely to be weaned from MV when treated with HFCWO vs. conventional physiotherapy [CPT] (Nduko et al. 1999). Moreover, HFCWO has been shown to be effective in improving secretion clearance in a population of adults /elderly patients who have been extubated after prolonged IMV [> 21 days] (Huang et al. 2013).

Despite these positive results, the application of HFCWO did not increase the success rate of weaning after extubation. Nowadays data on the application of HFCWO to patients on IMV are few; to date, only five trials have been published. Comparing HFCWO and CPT (percussion technique and postural drainage) in 9 intubated patients, Whitman and coworkers found no differences in the amount of sputum and in arterial oxygen saturation (SpO2), heart rate and arterial pressure (Whitman et al. 1993). Similarly, Unoki and colleagues did not find significant improvement in clinical outcomes [oxygenation, alveolar ventilation, and removal of secretions] (Unoki et al. 2005). Clinkscale and collaborators applied HFCWO to critically ill patients admitted to a Respiratory Intensive Care Unit and found that, compared to CPT, HFCWO is associated with lower values of pain assessment scores (Clinkscale et al. 2011). The authors found no significant differences between the two treatment groups with regard to the length of stay in ICU or hospital. The major limitation of this study was that only a minority of enrolled subjects was intubated at the time of treatment with HFCWO. More recent trials have shown a positive impact of the technique on clinical outcomes. The results of the Taiwanese RCT enrolling patients intubated because of severe acute respiratory failure secondary to pneumonia showed that HFCWO produces short-term adverse effects on SpO2, while not significantly altering Ppeak, minute ventilation, systolic pressure and heart rate (Chuang et al. 2017). In all patients, the mobilisation of endobronchial secretions was improved, but did not reach a statistically significant difference with respect to CPT. HFCWO is generally well tolerated, and the authors of the latter trial didn't detect significant changes in cardiorespiratory parameters. Similarly, Gugliotta et al. obtained a positive effect on secretion removal in invasively ventilated patients, as confirmed by changes in end-expiratory lung impedance [Deeli] (Gugliotta et al. 2016). Despite these promising results, to date, no large RCTs have been carried out to systematically analyse the possible beneficial effects or adverse events of HFCWO on the cardiorespiratory system. As a result, the applicability and safety of this physiotherapeutic technique among critically ill patients is still unknown, as well as its effectiveness.

Positive expiratory pressure (PEP) consists of a one-way valve through a mask or a mouthpiece connected to an adjustable expiratory resistor to enhance and promote secretion removal by stenting airways, increasing intrathoracic pressure, or increasing functional residual capacity (Myers 2007). The possible benefits of this technique are still under investigation (Örman and Westerdahl 2019), and its application to ICU patients is still to be studied.

> **"bed rest is a major problem associated with skeletal muscle weakness, disuse atrophy, and deconditioning"**

During last decades there has been increasing involvement of physiotherapists in the assessment and setting up of **non-invasive ventilation** (NIV), as the aims of respiratory physiotherapy and NIV frequently overlap (Ntoumenopoulos et al. 2011). Bilevel Positive Airway Pressure (BiPAP) is used predominantly for patients with exacerbations of COPD. However, there is an increasing application to patients who are at risk of post-extubation respiratory failure and also as part of a weaning strategy for patients with hypercapnic respiratory failure (Gosselink et al. 2008). Continuous Positive Airway Pressure (CPAP), BiPAP, or both are used for patients with acute cardiogenic pulmonary oedema and can also be used for selected patients with acute hypoxaemic respiratory failure from other aetiologies. NIV is known to decreased work of breathing and increase dynamic lung compliance, tidal volume, and inspiratory capacity with a subsequent improvement in blood gases. NIV can be a valuable complement to RP, which can be performed preferably during NIV sessions with a potential increase in patient's tolerance to efforts required by physiotherapy, in patient's co-operation. Moreover, the manipulation of the ventilator setting may facilitate the mobilisation and expulsion of secretions with potential improvement in lung mechanics and secretion expectoration. The strategies that can be adopted in intubated patient consist in generating lower inspiratory flows that translates into an increase in the difference in expiratory-inspiratory flows and categorically in the improvement of the transport of mucus. However, although there are encouraging results emerged from laboratory studies, the confirmations of this hypothesis in vivo are still few, and the application of NIV in order to facilitate secretion removal remains rare.

Another promising therapeutic option for critically ill patients is represented by **high flow nasal cannula** (HFNC). Since its introduction, HFNC has been applied to treat patients with hypoxaemic respiratory failure and to prevent reintubation in patients at risk of extubation failure (Maggiore et al. 2014; Hernández et al. 2016). In these patients, compared with conventional O_2 therapy, HFNC improves oxygenation, ameliorates the washout of pharyngeal dead space, reduces airway resistance, increases end-expiratory lung volume, and generation of positive airway pressure and decreases the work of breathing [WOB] (De Mussi et al. 2018). Moreover, HFNC is associated with greater comfort and tolerance, lower dyspnoea, lower dryness of upper airways and lower desiccation of secretions, compared to standard oxygen (Tiruvoipati et al. 2009; Rittayamai et al. 2013; Williams et al. 1996).

3. Mobilisation

During an acute phase of critical illness, the patient is usually confined in bed and, due to sedatives, he may not be collaborative. It's well known that bed rest is a major problem associated with skeletal muscle weakness,

disuse atrophy, and deconditioning (Stevens et al. 2007; Hermans et al. 2014). Drugs such as steroids and neuromuscular blockers exacerbate this critical illness neuromyopathy and malnutrition further compound this problem.

Indeed, early mobilisation of patients leads to improvements in peripheral and respiratory muscle strength, and, among patients treated with MV, it results in greater ventilation-free time (Wang et al. 2007). Mobilisation activates muscle metabolism and optimises oxygen transport by enhancing alveolar ventilation and ventilation/perfusion (V/Q) matching; it also represents a gravitational stimulus to maintain or restore circulation and normal fluid distribution in the body (Stiller et al. 2004; Dean 1994). Early mobilisation can be performed also in unconscious or sedated patients (Hanekom et al. 2011), and algorithms and protocols have been proposed as a guide in selecting eligible patients for mobilisation and providing appropriate treatment strategies (Liu et al. 2018). However, to date, there is insufficient evidence on the effects of early mobilisation of critically ill patients on physical function or performance, adverse events, muscle strength and health-related quality of life. This low-quality evidence is mostly due to small sample sizes, great variation, and inhomogeneities in the interventions and outcomes used to measure their effect. Nevertheless, the European Society of Intensive Care Medicine statement (Gosselink et al. 2008) suggests that active or passive mobilisation and muscle training should be instituted as soon as possible.

One of the interventions most frequently applied in the critical area is **body positioning** (Ambrosino et al. 2012). The physiological rationale for changing patient position is that it prevents dependent airway closure and atelectasis, pooling and stagnation of pulmonary secretions, and subsequent infection that may result from prolonged immobility (Raoof et al. 1999). In the supine position, lung volumes in dependent regions may reduce above functional residual capacity, leading to airway closure and atelectasis. At the same time airway resistance increases, mostly resulting from abdominal and chest wall compression, and this hinders the expulsion of secretions. In addition, the supine position, compared with the head-up position, has been found as a potential risk factor for pulmonary aspiration of gastric contents in patients receiving MV (Torres et al. 1992). Moreover, the semirecumbent or upright position (bed head positioned at 45°) is able to prevent pulmonary aspiration, to improve V/Q matching, lung volumes and mucociliary clearance, to reduce the respiratory rate, the WOB and the work of the heart, and to increase tidal volume and inspiratory flow rate (Gosselink et al. 2008; Zafiropoulos et al. 2004). Prone positioning has become an important instrument for the treatment of patients with ARDS, because it improves V/Q matching and oxygenation, redistributes oedema, and increases functional residual capacity (Jolliet et al. 1998; Mure et al. 1997). For patients with unilateral lung disease, placing the affected lung uppermost results in facilitating drainage from lung segments and improvement of V/Q matching.

> **“early mobilisation can be performed also in unconscious or sedated patients”**

Continuous lateral rotational therapy (CLRT) can be obtained through the use of specialised beds that rotate along the longitudinal axis, up to an angle of 60° onto each side, with a pre-set speed and degree of rotation (Traver et al. 1995). It has been hypothesised that CLRT can reduce the risk of sequential airway closure and pulmonary atelectasis, resulting in a reduction of lower respiratory tract infection and pneumonia, duration of endotracheal intubation and length of hospital stay (Ambrosino et al. 2012; Kirschenbaum et al. 2002). However, this therapy is not commonplace in the ICUs due to a lack of solid evidence of its cost-effectiveness. Adverse events are not common during positioning; however, as previously said, it's best to select the patient to treat considering individual specific risks and benefits of the process. Another important aspect to be considered is that prolonged immobility can determine joint contractures that limit the possibilities for future mobilisation. For patients who are unconscious passive limb exercises, such as stretching, splinting (Gosselink et al. 2008) or passive movements with continuous passive motion (CPM), should be applied daily as early as possible (Reid and McNair 2004; Griffiths et al. 2011). For patients who are conscious and able to follow instructions specific active therapy modalities involve any of the following: active turning and moving in bed, active-assisted and active exercises, pedal cycles in bed, tilt table, sitting at the edge of the bed, getting out of bed via mechanical lifting machines standing, transfers from bed to chair, chair-based exercises, and walking [with or without the help of standing or walking aids] (Sommers et al. 2015).

In conclusion, although there is unequivocal evidence that prolonged bed rest results in deconditioning, there is no published study, in patients receiving MV in ICU, investigating the effect of mobilisation on the pulmonary function, the weaning process, or the length of stay. However, the combination of multiple techniques involving mobilisation may result in the best clinical outcomes for patients admitted to an ICU (Ntoumenopoulos et al. 2002).

4. Muscular training

As previously said, critical patients are often forced to long periods of bed rest, with consequent progressive deconditioning and establishment of generalised muscle weakness. ICUAW is frequently observed in a substantial proportion of ICU-patients (Puthucheary et al. 2013; Nordon-Craft et al. 2012; Mendez-Tellez and Needham 2012). The prevalence of ICUAW is 25–40% in patients ventilated for ≥ 48 h and even higher in patients with sepsis or a prolonged ICU length of stay (LOS) (Appleton et al. 2015; De Jonghe et al. 1998; Tennilä et al. 2000). Muscle wasting develops since the very first week of illness, with more severity in patients with multiorgan failure compared with those with single organ failure (Puthucheary et al. 2013). ICUAW, including critical illness polyneuropathy, critical illness myopathy, and critical illness polyneuropathy and myopathy, is characterised by a profound weakness that is greater than normally expected from prolonged bed rest, and is therefore defined as clinically detected weakness in critically ill patients in whom

there is no plausible aetiology other than critical illness (Nordon-Craft et al. 2012; Hermans and Van den Berghe 2015; Kress and Hall 2014). This deficit in almost all cases involves skeletal muscles, but the respiratory muscles and diaphragm may also be profoundly altered. ICUAW limits the activities of daily living, and delays rehabilitation and recovery (Fan 2012; Herridge et al. 2011). Its possible aetiologies are mainly represented by deconditioning, disuse atrophy, systemic inflammatory response syndrome, sepsis, and multiple organ dysfunction syndrome, hyperglycaemia and medications [corticosteroids and neuromuscular blocking agents] (Hermans et al. 2014; Stevens et al. 2009). MV itself may adversely affect the diaphragm's structure and function, with a process termed ventilator-induced diaphragmatic dysfunction (Petrof et al. 2010). Indeed, patients who undergo prolonged periods of MV demonstrate a decrease in respiratory muscle endurance and are at risk of respiratory muscle fatigue (Chang et al. 2005).

Respiratory muscle weakness and, in particular, the imbalance between the muscle strength and load upon the respiratory system is one of the major determinants of weaning failure. However, the rationale of **respiratory muscle training (RMT)** in ICU is controversial, since little physiopathological information is available to support the specific use of respiratory muscles training among critical care patients. RMT has been associated with favourable weaning in ICU ventilatory-dependent COPD patients (Aldrich et al. 1989; Aldrich and Uhrlass 1987, Martin et al. 2002). The technique applied in these studies, **Inspiratory muscle training (IMT)**, targets the muscles of inspiration, namely the diaphragm and accessory inspiratory muscles, with the aim of increasing inspiratory muscle strength and endurance. In ventilated patients, the IMT device is incorporated into the ventilator circuit with an adaptor or connector, and IMT can be undertaken in several ways: isocapnic/normocapnic hyperpnoea training, resistive flow training, threshold pressure training, or adjustment of the ventilator to provide a training load for the inspiratory muscles. Since the results on the application of this technique in patients on IMV are controversial (Caruso et al. 2005), its routine use is not common.

With regard to peripheral muscles, during a period of inactivity, muscle mass declines and its efficiency to perform aerobic exercise is reduced. The effects of deconditioning are higher during the first week of immobilisation, when loss of strength reaches 40% (Bloomfield 1997). Muscular atrophy induced by bed rest is made worse by the association of critical illness polyneuropathy and malnutrition with protein wastage and bone demineralisation. Passive and active training of skeletal muscles in ICU should be aimed at restoring a muscle strength that allows basic daily life-activities and the ability to walk independently. For patients in critical conditions that cannot cooperate, **neuromuscular electrical stimulation (NMES)** is used to improve muscle performance. This therapy creates a passive contraction of skeletal muscles through the use of a low-voltage electrical impulse delivered through electrodes placed on the skin over the target muscle groups. The low-volt stimulation activates motor nerves

> **"patients who undergo prolonged periods of mechanical ventilation demonstrate a decrease in respiratory muscle endurance and are at risk of respiratory muscle fatigue"**

and mimics the effects of muscle contractions during mild exercise, with improvement in intramuscular blood flow, maximal muscle force output, and force endurance. Moreover, the repetitive contraction of muscle fibres helps in maintaining muscle tone. This passive training is generally well tolerated and was shown to significantly improve muscle strength and respiratory rate and decrease the number of days needed to transfer the patients from bed to chair among COPD patients receiving MV (Zanotti et al. 2003; Meesan et al. 2010; Williams and Flynn 2014). More recently the effects of NMES were studied with muscle ultrasounds in 26 critically ill patients; Gerovasilli et colleagues confirmed that this intervention is well tolerated and found out that it may help in preserving the muscle mass (Gerovasili et al. 2009). However, among critically ill patients the efficacy of NMES may be reduced, especially in patients having sepsis or oedema, or receiving vasopressors because these conditions might impede with the generation of a sufficient muscle contraction by electrical muscle stimulation (Segers et al. 2014; Fossat et al. 2018).

For patients in a more stable condition, the sessions of muscular training usually involve passive or active movements of lower and upper extremities, eventually enhanced by lifting light weights or pushing against resistance. Rehabilitation-related technologies, such as **cycle ergometer (CE)**, may play an important role in improving muscle strength and physical function in ICU patients. With this stationary cycling apparatus, patients can exercise through passive, active-assisted, or active training. Among sedated, immobile patients with severe critical illness CE may help in preserving muscle architecture (Griffiths 1997; Burtin et al. 2009). However, despite its potential benefits, rigorous evaluation of CE as a rehabilitation therapy for ICU-patients is still limited.

Later, as soon as the patient is able to stand, the physiotherapist should start progressive **walking retraining**, aided by a rolling walker if needed. Strategies include patient mobilisation based on a progressive sequence of activities like decubitus change and functional positioning, cycling and sitting in bed, and standing, static walking, transferring from bed to chair, and walking. Oxygen therapy or a portable NIV-respirator can eventually be used to decrease the WOB during walking. In a controlled trial, Nava et al. showed that the application of a step-by-step peripheral muscle retraining program to COPD patients recovering from an acute episode of hypercapnic respiratory failure and admitted in ICU has been associated with improvement in the patient's exercise capacity and symptoms score as compared to controls (Nava 1998).

Conclusions

Patients who survive hospitalisation in ICU are at increased risk for reporting nega-

tive complications of critical illness, even after stabilisation of the conditions. They frequently develop neuromuscular, cognitive and psychosocial deficits which can result in decreased quality of life, impaired ability to function autonomously and altered occupational performance. This significant morbidity represents a burden to patients, caregivers, and society.

In recent years the profile of rehabilitation in critical illness to mitigate these long-lasting complications has increased, and respiratory rehabilitation has become a cornerstone in the comprehensive management of ICU-patients. There is growing evidence that an early and progressive programme is feasible with low risk to the patient. Respiratory physiotherapy determines recognised short-term benefits, preventing some ICU complications, such as PICS and ICUAW, and preserving or recovering patients' functionality. The treatment strategies should be applied in the early phase of illness, as soon as the patient reaches cardiorespiratory and neurological stabilisation. Even sedated and not collaborative patients can be passively treated. Respiratory physiotherapy programmes are usually based in four areas:

> **an early and progressive program of respiratory physiotherapy is feasible with low risk to the patient**

lung hyperinflation, drainage of endobronchial secretions, mobilisation and muscle training. Benefits potentially associated with respiratory physiotherapy include shortening of the weaning time, restoration of functional capacity and physical independence, reduction of length of stay and healthcare costs. However, no significant effects have been shown on cognitive function or mortality.

A multidisciplinary team approach (physical therapist, physician, nurse) is fundamental to conduct a safe and effective rehabilitation programme.

With a growing population of ICU survivors, greater standardisation of respiratory physiotherapy techniques is needed, especially given the unique challenges presented by ICU patients and the environment. There is great potential for exploring the benefits of interventions, and we encourage for large scale, rigorous randomised trials to further explore long-term outcomes and the ideal dose and timing and the effect of specific techniques on specific conditions. Furthermore, we need to improve ICU organisation and teams to be able to deliver early intervention. ■

References

Bailey P, Thomsen GE, Spuhler VJ, et al. (2007) Early activity is feasible and safe in respiratory failure patients. Crit Care Med, 35(1):139-45.

Barnato AE, Albert SM, Angus DC, Lave JR, Degenholtz HB (2011) Disability among elderly survivors of mechanical ventilation. Am J Respir Crit Care Med, 183(8):1037-42.

Berney S, Denehy L (2003) The effect of physiotherapy treatment on oxygen consumption and haemodynamics in patients who are critically ill. Aust J Physiother, 49(2):99-105.

Berney S, Haines K, Denehy L (2012) Physiotherapy in critical care in Australia. Cardiopulm Phys Ther J, 23(1): 19–25.

Bourdin G, Barbier J, Burle J-F, et al. (2010) The feasibility of early physical activity in intensive care unit patients: a prospective observational one-center study. Respir Care, 55(4):400-7.

Brummel NE, Girard TD, Ely EW, et al. (2014) Feasibility and safety of early combined cognitive and physical therapy for critically ill medical and surgical patients: The Activity and Cognitive Therapy in ICU (ACT-ICU) trial. Intensive Care Med, 40(3):370-9.

Cavalcanti AB, Suzumura ÉA, Laranjeira LN, et al. (2017) Effect of lung recruitment and titrated Positive End-Expiratory Pressure (PEEP) vs low PEEP on mortality in patients with acute respiratory distress syndrome - A randomized clinical trial. J Am Med Assoc, 318(14):1335-1345.

Chan KS, Aronson Friedman L, Dinglas VD, et al. (2016) Evaluating physical outcomes in acute respiratory distress syndrome survivors: Validity, responsiveness, and minimal important difference of 4-meter gait speed test. Crit Care Med, 44(5):859-68.

Cirio S, Piaggi GC, De Mattia E, Nava S. (2003) Muscle retraining in ICU patients. Monaldi Arch chest Dis = Arch Monaldi per le Mal del torace, 59(4):300-303.

Clarke RCN, Kelly BE, Convery PN, Fee JPH (1999) Ventilatory characteristics in mechanically ventilated patients during manual hyperventilation for chest physiotherapy. Anaesthesia, 54(10):936-940.

Cox CE, Martinu T, Sathy SJ, et al. (2009) Expectations and outcomes of prolonged mechanical ventilation. Crit Care Med, 37(11):2888-94.

Denehy L (1999) The use of manual hyperinflation in airway clearance. Eur Respir J, 14(4):958-65.

Dinglas VD, Aronson Friedman L, Colantuoni E, et al. (2017) Muscle Weakness and 5-Year Survival in Acute Respiratory Distress Syndrome Survivors, Crit Care Med.45(3):446-453

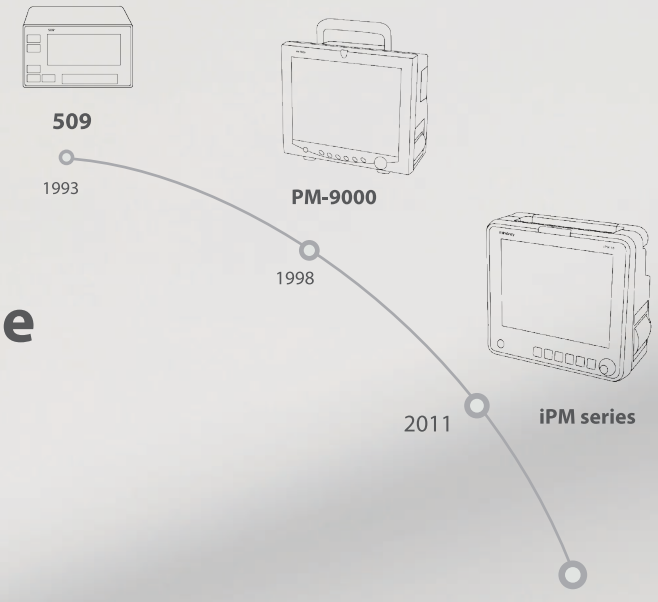
Elliott D, Davidson JE, Harvey MA, et al. (2014) Exploring the scope of post-intensive care syndrome therapy and care: Engagement of non-critical care providers and survivors in a second stakeholders meeting. Critical Care Medicine, 42(12):2518-26.

For full references, please email editorial@icu-management.org or visit https://iii.hm/u6l

Abbreviations

ARDS	acute respiratory distress syndrome
BiPAP	bilevel positive airway pressure
CE	cycle ergometer
CLRT	continuous lateral rotational therapy
COPD	chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
CPM	continuous passive motion
CPT	conventional physiotherapy
FiO2	fractional concentration of inspired oxygen
HFCWC	high-frequency chest wall compressions
HFCWO	high-frequency chest wall oscillations
HFNC	high flow nasal cannula
HFOs	high-frequency oscillations
HFV	high-frequency ventilation
IAMW	ICU-acquired muscle weakness
ICUAW	intensive care unit-acquired weakness
ICP	intracranial pressure
ICU	intensive care unit
IMT	inspiratory muscle training
IMV	invasive mechanical ventilation
IPV	intrapulmonary percussive ventilation
MAP	mean arterial pressure
MHI	manual hyperinflation
MV	mechanical ventilation
NIV	non-invasive ventilation
NMES	neuromuscular electrical stimulation
PEP	positive expiratory pressure
PEEP	positive end-expiratory pressure
PICS	post-intensive care syndrome
RASS	Richmond agitation sedation scale
RCT	randomised controlled trial
RM	recruitment manoeuvres
RMT	respiratory muscle training
RP	respiratory physiotherapy
VAP	ventilator-associated pneumonia
VHI	ventilator hyperinflation
WOB	work of breathing

mindray



26 years of heritage and innovation

ePM™ series

The Evolution of Simplicity

Mindray patient monitors, inspired by the need of customers, adopt advanced technologies and transform them into accessible innovation. The ePM delivers excellent visual experience, intelligent operation experience, accurate physiological measurement, smooth workflow, valuable and accessible IT solutions for various hospital settings.

Tim Frenzel
Radboudumc Centre of Expertise for Weaning from Mechanical Ventilation
Department of Critical Care Medicine
Radboud University Nijmegen Medical Centre
The Netherlands

Tim.Frenzel@radboudumc.nl

@horstie
@NExCOB

Lisanne Roesthuis
Radboudumc Centre of Expertise for Weaning from Mechanical Ventilation
Department of Critical Care Medicine
Radboud University Nijmegen Medical Centre
The Netherlands

Lisanne.Roesthuis@radboudumc.nl

Johannes G van der Hoeven
Radboudumc Centre of Expertise for Weaning from Mechanical Ventilation
Department of Critical Care Medicine
Radboud University Nijmegen Medical Centre
The Netherlands

Hans.vanderHoeven@radboudumc.nl

www.radboudumc.nl/ontwennen-beademing

A structural approach for diagnosing weaning failure

A case from a specialised weaning centre

Using a case of a former patient we describe the structured approach of analysis of the cause of weaning failure with corresponding specific therapies used in our Centre for Expertise.

Previously, we suggested a structural approach for diagnosing the cause of weaning failure (Heunks and van der Hoeven 2010; Schellekens et al. 2016). Here we discuss how we apply 'the ABC of weaning failure' at the Radboudumc Centre of Expertise for Weaning from Mechanical Ventilation using the case of a former patient. At our centre patients are admitted who failed previous weaning trials. Once a patient is admitted to the weaning centre, the first aim is to establish a firm diagnosis for the cause(s) of weaning failure. When the cause(s) are clarified, an individualised strategy for treating the patient is determined.

Our centre for expertise consists of 4 beds (expanding) and has a staff consisting of intensive care nurses, residents, and intensivists. In the multidisciplinary team, physiotherapists and speech-language therapists (SLTs) play an important role besides other consultants (e.g. neurologist, psychiatrist, ENT specialist, rehabilitation medicine or pulmonologist). For mobilisation of our ventilated patients we use - besides regular training - our specialised gymnasium and our swimming pool (hydrotherapy), **Figure 1a** (Felten-Barentsz et al. 2015).

Case

We describe the case of a 65 year old female referred to our unit from another hospital with prolonged mechanical ventilation of 13 days and multiple unsuccessful spontaneous breathing trials (SBTs).

She had a history of hypertension, cardiac failure (unclear aetiology) and peripheral and central vascular disease for which she had multiple times surgery (among others placement of an aortic bifurcation prosthesis with multiple revisions). She suffered from recurrent pleural and pericardial effusion.

The patient was admitted to the referring hospital 3 weeks previously with dyspnoea and signs of cardiac failure. A pleural centesis was complicated by haematothorax leading to haemodynamic instability and admission to the ICU. During the ICU admission in the referring hospital, she had recurrent pleural and pericardial effusion and acute-on-chronic kidney failure for which she needed renal replacement therapy. Intermittent hypertension appeared difficult to control.

In our unit, physical examination showed bilateral basal crackles with a regular heart rhythm and a systolic murmur. She had a soft, nontender, distended abdomen. She had generalised oedema and a sacral decubitus wound. She was ventilated with pressure support mode (PS) 20 above 8 cmH_2O positive end-expiratory pressure (PEEP), tidal volume ca. 420 mL, spontaneous respiratory rate 30/min, FiO_2 0.50.

Our structured approach for the causes of weaning failure showed the following during a SBT using a T-piece trial:

Airway and lung dysfunction

Factors increasing the work of breathing and thereby contributing to weaning failure, are increased airway resistance, decreased lung or chest wall compliance and impaired gas exchange.

Increased airway resistance may be due to the endotracheal tube and central or smaller airways. Sputum retention or plug can be a problem in the endotracheal tube or central airways, and tracheomalacia or tracheal stenosis can also cause obstruction in the central airways. Both can be visually inspected by performing a flexible bronchoscopy. Increased resistance of smaller airways can be a problem in patients with chronic obstructive pulmonary disease (COPD) and is associated with the development of intrinsic positive end-expiratory pressure (PEEPi). Increased airway resistance can also develop in patients failing during a T-piece trial (Jubran and Tobin 1997). Intrinsic PEEP is measured during controlled ventilation by performing an end-expiratory occlusion manoeuvre and during assisted ventilation by measuring the drop in oesophageal pressure (Pes) before inspiratory flow begins.

Table 1 shows the results for these measure-

Figure 1. left, **a:** hydrotherapy with a ventilated patient. right, **b:** physiotherapy with family participation in a weaning patient.

Respiratory parameter	SBT duration (minutes)				
	5	30	60	120	180
Respiratory rate [breaths/minute]	32	31	32	31	32
Tidal volume [mL]	296	287	313	295	388
Minute ventilation [L/minute]	9.4	8.9	9.9	9.2	12.1
Δ Pes [cmH_2O]	-15.9	-14.2	-16.0	-18.4	-21.4
Δ Pga [cmH_2O]	5.5	4.9	3.6	1.6	4.2
Δ Pdi [cmH_2O]	*21.4*	*19.1*	*19.6*	*20.0*	*25.6*
PEEPi [cmH_2O]	*3.5*	*2.7*	*2.6*	*2.9*	*3.5*
Δ EAdi [μV]	10.9	10.3	13.3	16.4	20.8
Dynamic lung compliance [mL/cmH_2O]	*39.3*	*40.3*	*36.4*	*30.8*	*43.3*
Airway resistance [cmH_2O/L/s]	*16*	*15*	*17*	*19*	*19*
NMEx [cmH_2O/μV]	*2.0*	*1.9*	*1.5*	*1.2*	*1.2*
NVE [mL/μV]	27.2	27.9	23.5	18.0	18.7
WOB [J/L]	*1.3*	*1.2*	*1.3*	*1.5*	*1.8*

Table 1. Respiratory parameters during the course of a SBT.

SBT = spontaneous breathing trial; Pes = oesophageal pressure; Pga = gastric pressure; Pdi = transdiaphragmatic pressure; EAdi = electrical activity of the diaphragm; NME = neuromechanical efficiency; NVE = neuroventilatory efficiency; WOB = work of breathing

	Start SBT	1 hour SBT
pH	7.47	7.44
$PaCO_2$ [mmHg]	41	49
PaO_2 [mmHg]	*117*	*67*
HCO_3- [mmol/L]	29.0	31.9
Base excess [mmol/L]	4.8	6.9
SaO_2 [%]	98	93
E [cm/s]	113	140
A [cm/s]	128	100
E/A	*0.88*	*1.40*
E'[cm/s]	7.00	6.59
E/E'	*16.1*	*21.2*

Table 2. Bloodgas and echocardiography results before and after a SBT.

ments. Our patient had a low *dynamic lung compliance* of 30 to 44 (normal compliance range 60-100) mL/cmH_2O, which remained constant during the SBT. A low lung compliance can have several causes, such as lung oedema, pneumonia or hyperinflation. We found a small amount of *PEEPi*, remaining constant during the SBT and therefore we could exclude hyperinflation. The *airway resistance* was normal and remained constant during the SBT, therefore we concluded that this did not play a major role in the weaning problem.

Brain dysfunction

Brain dysfunction is associated with a higher risk of failed extubation and *anxiety* and *depression* may interfere with successful weaning (van den Boogard et al. 2012).

Our patient was suffering from anxiety but did not show signs of *delirium* (CAM-ICU) or depression . She did have an acceptable *sleep quality* (NRS), (Rood et al. 2019). We regularly try to avoid benzodiazepines. Regarding management of anxiety interventions as cognitive behavioural therapy and the professional and patient attendance by our team of ICU nurses play an important role.

Cardiac dysfunction

The conversion from mechanical ventilation to spontaneous breathing leads to changes in intrathoracic pressure affecting ventricular pre- and afterload and a necessary increase

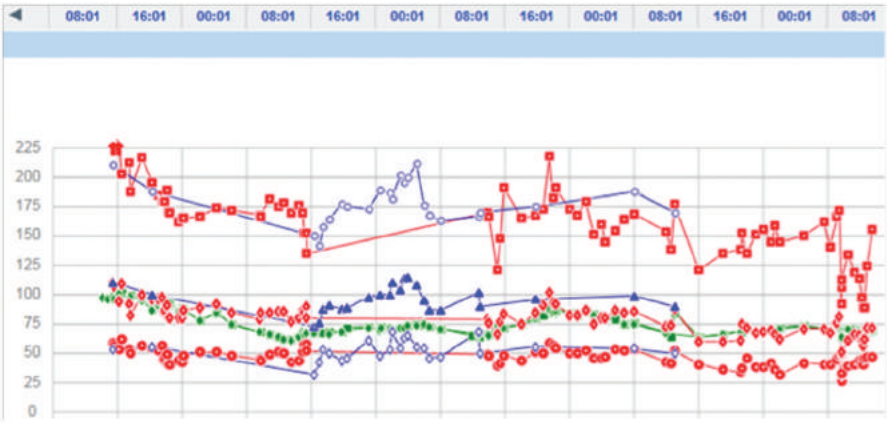


Figure 2. Blood pressure (arterial, red and non-invasive, blue [mmHg]); heart rate (green [/min]) over time showing better blood pressure control with intensified therapy (AT2-agonist, nitroglycerin, and intensive fluid removal)

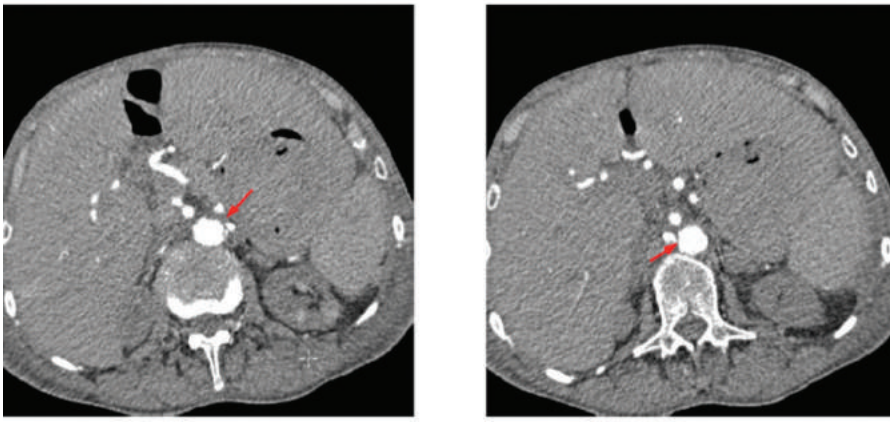


Figure 3. CT angiogram: severe stenosis at the origin of the left (a) and right (b) renal artery

in cardiac output due to increased oxygen consumption by respiratory muscles (Dres et al. 2014).

Cardiac function can be investigated non-invasively by electrocardiography (ECG) and echocardiography. An increase in brain natriuretic peptide (BNP, increase of ≥ 48 ng/L or ≥ 12%) during weaning is also a reliable sign of a cardiac cause of weaning failure. If this does not clarify the problem, a pulmonary arterial catheter can be inserted to measure pulmonary arterial occlusion pressure and cardiac index. Transpulmonary thermodilution may be used to determine extravascular lung water (increased when ≥ 14%) (Lemaire et al. 1988; Dres et al. 2014).

NT-proBNP level of our patient was >35000 (normal <300) pg/mL before and after a SBT. Although we could not determine an increase during weaning, a cardiac cause for weaning failure was suspected.

Her *ECG* did not show signs of ischaemia before and after a SBT. Thus cardiac ischaemia as a cause of weaning failure was deemed to be unlikely.

Echocardiography showed an enlarged left atrium with a hypertrophic left ventricle with good contractility without segmental wall motion abnormalities and a good right ventricular function. The aortic annulus showed calcification without stenosis, a minimal tricuspid insufficiency was seen with an estimated pulmonary systolic pressure of 50-55 mmHg. There was an increase in E/A and E/E' after the SBT compared to before consistent with congestive heart failure with preserved ejection fraction (diastolic dysfunction, **Table 2**). Treatment consisted of afterload reduction by blood pressure control and intensive fluid removal via haemofiltration.

Our patient had a decrease in PaO_2 after 1 hour SBT (**Table 2**). At this point haemofiltration with fluid removal was initiated (more than 3 L) which led to improvement of SpO_2, thus the SBT could eventually be continued until the evening (7 hours). This course was consistent with our final conclusions.

Our patient suffered from a difficult to treat hypertension (**Figure 2**). Regarding the difficulty of blood pressure control also in the referring hospital, we felt the need to exclude a renal cause of hypertension by means of a contrast CT scan, which showed severe stenosis at the origin of the left and the right renal artery (**Figure 3**). After consulting the nephrologist and the interventional radiologist, we concluded that there was no invasive treatment possible due to atherosclerosis and risk of complications and that the patient would need chronic haemodialysis. We focussed on medical treatment of hypertension with an AT2-antagonist (allergy for ACE inhibitor), nitroglycerin during SBTs (Routsi et al. 2010) and on fluid removal using haemodialysis.

Diaphragm/respiratory muscle function

During mechanical ventilation respiratory muscle dysfunction rapidly develops and is associated with difficult weaning (Jaber et al. 2011; Hooijman et al. 2015; Goligher et al. 2018). Importantly, diaphragm weakness is not the same as intensive care unit acquired weakness (Dres et al. 2017), in other words, the diaphragm can be weak without peripheral muscle weakness and vice versa. Therefore, respiratory muscle function itself should be monitored (Doorduin et al. 2013). It can be monitored using different techniques; here we will focus on measuring the electrical activity of the diaphragm (EAdi) and transdiaphragmatic pressure (Pdi; computed as gastric (Pga) minus oesophageal (Pes) pressure).

In our patient, a T-piece trial was performed while measuring flow, EAdi, Pes, and Pga. She had a relatively high respiratory rate with low tidal volumes (**Table 1**). *EAdi* varied between 10 – 21 μV, which can be considered normal. The inspiratory decrease in *Pes* was moderate to high (13 – 19 cmH_2O), while the inspiratory increase in *Pga* was also high (3.3 – 7.0 cmH_2O), resulting in a Pdi (18 – 25 cmH_2O) higher than cut-off values defining diaphragm weakness (i.e. 11 cmH_2O) (American Thoracic Society/European Respiratory 2002). In addition, *neuromechanical efficiency* (NME; i.e.

Pdi/EAdi) was relatively high (Doorduin et al. 2018). These respiratory parameters indicate that there was no sign of *diaphragm weakness*. Furthermore, the patient had a *high breathing effort* (normal range work of breathing (WOB) 0.2-0.9 J/L) mainly due to a low *dynamic lung compliance* (**Table 1**). In this patient, there was no need for inspiratory muscle training (Martin et al. 2002).

Endocrine and metabolic dysfunction

Adrenal insufficiency (Huang and Lin 2006) and hypothyroidism (Datta and Scalise 2004) have been described as possible reasons for weaning failure accompanied by successful treatments though the literature is scarce. Our patient had a normal TSH 1.76 (normal range 0.27-4.2) mE/L. Aldosterone level was elevated 0.87 (normal range 0.08 - 0.69) nmol/L. Renin level was increased as well 120 (normal range 4.4 – 85) mU/L matching with the diagnosis of renal artery stenosis. A short ACTH test showed an adequate reaction (baseline 0.65, 30 min 0.89 and 60 min 0.97 µmol/L).

Feeding and dysphagia

Malnutrition frequently occurs in critically ill patients and is associated with higher mortality (Mogensen et al. 2015) and reduced muscle mass contributing to difficult weaning. During spontaneous ventilation patients have an increased energy expenditure compared to controlled ventilation (Hoher et al. 2008). Patients ventilated more than 48 hours have a high risk of dysphagia (Skoretz et al. 2010), which has a relation with duration of intubation, age, muscle weakness, and neurological diseases. Screening for *dysphagia* after extubation by ICU nurses or SLTs improves oral intake (See et al. 2016). Fibreoptic endoscopic evaluation of swallowing (FEES) can help in the work-up (Scheel et al. 2016).

We use indirect calorimetry to estimate individual necessary intake of calories (our patient 1894 kCal/day) and an estimate for targeted protein intake (1.2-1.5 g/kg/d). Our patient was fed via a nasogastric tube. She did not have signs of dysphagia after extubation, and oral intake could be increased.

Conclusion

In our opinion, an individualised structural evaluation of weaning failure helps to find the underlying causes of weaning failure and to prescribe an individualised treatment plan. We think that our patients benefit from separating our more acute care ICUs from this specialised unit, being able to focus on a different kind of patient with a dedicated staff (**Figure 1b**). We recently showed that difficult to wean patients treated at our unit had a high rate of successful weaning (79%) (Frenzel 2018). Our patients were vulnerable before admission with an increase of their frailty at discharge improving modestly after 3 months (clinical frailty score), while mental health was comparable to the situation before admission (SF 36). However, we do not know yet what the relevance of this approach is regarding the whole population of patients with prolonged mechanical ventilation and weaning failure in terms of outcome parameters such as ventilator-free days, mortality or quality of life. Currently, the MONITOR-IC study is investigating the effects and consequences of ICU admission on quality of life during five years after ICU admission (Geense et al. 2017). Also, patients admitted to our weaning centre are included in this study, and we hope to be able to report these results soon.

The identified factors for weaning failure that played a role in our described patient were:

- CHF with preserved ejection fraction (diastolic dysfunction)
- Acute-on-chronic kidney failure
- Difficult to treat hypertension due to renal artery stenosis
  - Leading altogether to peripheral and lung oedema

She was treated with:

- No angiographic/surgical intervention due to severe atherosclerosis with increased risk of complications
- Intensive fluid removal with haemodialysis (total negative fluid balance 9.6 L)
- Nitroglycerin during SBT (systolic blood pressure < 150 mmHg) to prevent CHF due to increased afterload
- Treatment of hypertension with AT2 antagonist

Our patient could be successfully weaned from the ventilator and extubated within 4 days. ■

Key points

- Factors increasing the work of breathing and thereby contributing to weaning failure, are increased airway resistance, decreased lung or chest wall compliance and impaired gas exchange.
- Brain dysfunction is associated with a higher risk of failed extubation and anxiety, sleep disturbances and depression may interfere with successful weaning.
- During mechanical ventilation respiratory muscle dysfunction rapidly develops and is associated with difficult weaning, but not with peripheral muscle weakness.
- Adrenal insufficiency and hypothyroidism have been described as possible reasons for weaning failure accompanied by successful treatments.
- Malnutrition frequently occurs in critically ill patients and is associated with higher mortality and reduced muscle mass contributing to difficult weaning.
- An individualised structural evaluation of weaning failure helps to find the underlying causes of weaning failure and to prescribe an individualised treatment plan.

References

American Thoracic Society/European Respiratory S (2002) ATS/ERS Statement on respiratory muscle testing. Am J Respir Crit Care Med, 166(4): 518-624.

Datta D. and P Scalise (2004) Hypothyroidism and failure to wean in patients receiving prolonged mechanical ventilation at a regional weaning center. Chest, 126(4): 1307-1312.

Doorduin J, Roesthuis LH, Jansen D, van der Hoeven JG, van Hees HWH, Heunks LMA. (2018) Respiratory muscle effort during expiration in successful and failed weaning from mechanical ventilation. Anesthesiology, 129(3): 490-501.

Doorduin J, van Hees HWH, van der Hoeven JG, Heunks LMA. (2013) Monitoring of the respiratory muscles in the critically ill. Am J Respir Crit Care Med, 187(1): 20-27.

Dres M, Dubé BP, Mayaux J, Delemazure J, Reuter D, Brochard L, Similowski T, Demoule A (2017) Coexistence and impact of limb muscle and diaphragm weakness at time of liberation from mechanical ventilation in medical intensive care unit patients. Am J Respir Crit Care Med,195(1): 57-66.

Dres M, Teboul JL, Anguel N, Guerin L, Richard C, Monnet X (2014) Extravascular lung water, B-type natriuretic peptide, and blood volume contraction enable diagnosis of weaning-induced pulmonary edema. Crit Care Med, 42(8): 1882-1889.

Dres M, Teboul JL, Monnet X (2014) Weaning the cardiac patient from mechanical ventilation." Curr Opin Crit Care 20(5): 493-498.

Felten-Barentsz KM, Haans AJ, Slutsky AS, Heunks LM, van der Hoeven JG (2015) Feasibility and safety of hydrotherapy in critically ill ventilated patients. Am J Respir Crit Care Med 191(4): 476-477.

Frenzel T, Roesthuis LH, van den Boogard M, Zegers M; van der Hoeven JG (2018) Preliminary results of the first dedicated Dutch ICU for complex weaning from mechanical ventilation. 6th European Conference on Weaning and Rehabilitation in Critically Ill Patients. Leuven.

Geense W, Zegers M, Vermeulen H, van den Boogaard M, van der Hoeven J. (2017) "MONITOR-IC study, a mixed methods prospective multicentre controlled cohort study assessing 5-year outcomes of ICU survivors and related healthcare costs: a study protocol. BMJ Open 7(11): e018006.

For full references, please email editorial@icu-management.org or visit https://iii.hm/u6l

Vitamin D deficiency in ICU patients

A review on the role of vitamin D in a well-defined setting of critically ill patients: patients undergoing cardiac surgery and organ transplantation, and the potential benefit of vitamin D supplementation.

Gennaro Martucci
Department of Anesthesia and Intensive Care
IRCCS-ISMETT (Istituto Mediterraneo per i Trapianti e Terapie ad alta specializzazione)
Palermo, Italy

gennaro.martucci@libero.it

Karin Amrein
Department of Internal Medicine
Division of Endocrinology and Diabetology
Medical University of Graz
Graz, Austria

karin.amrein@medunigraz.at

Julia Ney
Department of Intensive Care Medicine and Anesthesiology
Medical Faculty
RWTH Aachen University
Aachen, Germany

ney.julia1@gmail.com

Vitamin D research has experienced a true hype in all fields of medicine in the last decades. In critical illness, this increased interest has only started 10 years ago. The high prevalence of vitamin D deficiency in critically ill patients and the rationale for a modulating role of vitamin D in acute illness but also long-term outcomes is certainly intriguing. However, vitamin D is no panacea, so it is not surprising that even large studies like the recent VITAL trial were unable to demonstrate an effect of vitamin D in a relatively healthy and largely vitamin D replete population (Manson et al. 2019).

So far, the Austrian VITdAL-ICU trial was the largest RCT (n= 480) to test the hypothesis that high dose cholecalciferol supplementation in a mixed population of critically ill patients with vitamin D deficiency may rapidly restore plasma vitamin D concentrations and improve clinical outcomes. The primary endpoint, hospital length of stay, was similar between groups, but mortality was substantially and significantly lower in patients with severe vitamin D deficiency.

In this short review, we will focus on the role of vitamin D in a well-defined setting of critically ill patients: patients undergoing cardiac surgery and organ transplantation. We will highlight the rationale for the potential benefit of vitamin D supplementation and briefly discuss the ongoing large intervention trials in the ICU setting.

> **vitamin D deficiency is associated with greater illness severity, morbidity, and mortality in both paediatric and adult critically ill patients**

Vitamin D and acute illness/ mortality/immune function

Vitamin D is a pre-hormone acting via its metabolite 1,25-dihydroxy vitamin D3, with direct and indirect effects in most human tissues and cell types. The best studied actions of vitamin D include the modulation of bone and muscle metabolism, and a number of non-classical and pleiotropic wide-ranging biological effects. Several studies have recognised how vitamin D deficiency is associated with greater illness severity, morbidity, and mortality in both paediatric and adult critically ill patients. Vitamin D works through endocrine, autocrine, and paracrine actions that activate a variety of rapid effects, but also a number of signaling pathways and human epigenomic responses that probably need days to become effective. Given its actions, vitamin D has the potential to represent an independent, modifiable risk factor amendable to rapid normalisation through loading dose supplementation.

Vitamin D3 (cholecalciferol), is absorbed from food sources or produced by the skin in the presence of sunlight. After being metabolised by the liver into 25-hydroxy-vitamin D [25(OH)D] and further converted to its biologically active form 1,25-dihydroxy-vitamin-D [1,25(OH)2D] by the kidneys within 2-3 days, it binds with high affinity to the vitamin D receptor (VDR) in many organs. Besides its well-known effects on calcium homeostasis and bone health, vitamin D shows immunomodulating (Sassi et al. 2018), and organ protective properties (Amrein et al. 2018). Moreover, ICU patients, especially patients undergoing cardiopulmonary bypass surgery and transplant patients appear to be at high risk for developing osteoporosis and fragility fractures in the long term, and vitamin D deficiency is an important risk factor.

Vitamin D deficiency - generally defined as 25(OH)D serum levels lower than 20 ng/mL (equals 50 nmol/l) - is reported in 40 to 70% of all ICU patients (Amrein et al. 2018), and is even more common after transplant surgery with a prevalence of 50 to 90% (Thiem et al. 2013). It is associated with an increased risk of mortality, organ dysfunction, infections, prolonged ICU and hospital stay as well as increased duration of mechanical ventilation in several observational trials (Amrein et al. 2014a; de Haan et al. 2014).

While VITDAL-ICU, the largest prospective interventional trial including 480 critically ill patients failed to show an overall beneficial effect of high dose (540.000 IU oral cholecalciferol) supplementation in the general

ICU population, a significantly reduced risk of 28-day mortality was observed in a subgroup of patients with severe 25(OH)D deficit <12 ng/mL (equals 30 nmol/l) (Amrein et al. 2014b).

Patients receiving prehospital vitamin D supplementation have significantly shorter ICU stay, fewer days of mechanical ventilation and lower rates of mortality (Leclair et al. 2019), supporting the importance of the availability of biologically active vitamin D at the time of acute illness.

Vitamin D and cardiac surgery

Within cardiac surgery patients, 40 to 80% demonstrate 25(OH)D levels lower than 20ng/mL preoperatively and experience a significant intraoperative decrease in biologically active vitamin D serum levels (Ney et al. 2018). Preoperative malnutrition, poor general health, limited sunlight exposure, and preexisting liver and kidney dysfunction are primary causes of vitamin D deficiency in this cohort. Open heart surgery is associated with alarming complication rates (15-20%) and mortality rates of about 3-4% (Herman et al. 2013). The significant systemic inflammation can cause severe organ injury and dysfunction resulting in serious life-threatening complications. The setting of inflammation additionally leads to a downregulation of 25(OH)D and 1,25(OH)2D by the enzyme 24-hydroxylase and a reduction of the vitamin D binding protein with as a result lower serum levels (Al Tarrah et al. 2018). Vitamin D is involved in the regulation of the immune system, modulates the endothelial function and has an effect on arterial stiffness. The exact mechanism of action is still being investigated. However, 1,25-dihydroxy-vitamin-D triggers an upregulation of antibacterial peptides such as cathelicidin by macrophages and monocytes, which in turn is capable of eradicating infectious cells. Active immune cells can locally convert 25(OH)D into the active form of vitamin D in order to provide immunoprotective properties. Furthermore, 1,25(OH)2D activates several anti-inflammatory mediators (e.g. IL-4 and IL-10) and inhibits pro-inflammatory cytokines such as interferon, interleukin 2 and 6 and tumour necrosis factor (Sassi et al. 2018; Ramos-Martinez et al. 2018). These cardioprotective properties have been shown to improve clinical outcome after cardiac surgery.

Several observational studies showed that low preoperative 1,25(OH)2D levels are associated with an increased risk of organ dysfunctions and infections in cardiac surgery patients (Ney et al. 2018; Zittermann et al. 2016). In addition, vitamin D deficient cardiac surgery patients showed a significantly higher frequency of postoperative atrial fibrillation and major adverse cardiac and cerebrovascular events. Although some studies show a correlation between low preoperative vitamin D levels and mortality (Zittermann et al. 2013), others were not able to replicate these results (Turan et al. 2013). Since there are many factors influencing mortality rates such as the preoperative health condition, the surgical procedure itself and the cardiopulmonary bypass time, vitamin D's role remains unclear. Even though vitamin D deficiency is extremely prevalent in this patient cohort and supplementation might help to improve clinical outcome after cardiac surgery, no intervention trials have been carried out so far. Future studies are needed to address this issue.

Vitamin D and organ transplantation

Several studies have highlighted that lower 25-hydroxyvitamin D levels at ICU admission, also in post-surgical ICU, are associated with prolonged hospitalisation, ICU readmission, and mortality.

Given its wide immunobiological effects, vitamin D has been frequently considered a potential modulating factor after solid organ (and stem cell) transplantation (mainly liver, kidney and lung). The transplantation recipient population is particularly prone to infections, mainly in the early stage after transplantation, due to immunomodulation/chronic immunosuppressive therapy and to long term bone dysfunction.

The reasons for insufficient vitamin D levels in the transplant setting are manifold and comprise limited sunlight exposure and reduced dietary intake of vitamin D containing food as well as liver and kidney dysfunction.

In liver transplantation recipients, osteoporosis has a high prevalence with a large decline in bone mineral density in the first year after transplantation. Vitamin D levels are often very low in liver recipients. Moreover, a negative association between low vitamin D levels and graft function as well as a role of vitamin D in reducing the recurrence of hepatitis C virus infection has been demonstrated. In a recent cohort of Swiss liver recipients, the pre-transplantation vitamin D status was associated with the incidence of infections in the first 6 months.

The modulating effect of vitamin D and the presence of its specific receptor in almost all cells and tissues of the human body, with the preliminary data on low vitamin D status and outcome call for an action in this field to understand if vitamin D is only a "bystander" (just a marker of disease) or if it is a potential modulator of clinical trajectories in this specific setting.

The future

The two large ongoing vitamin D supplementation trials in general critical illness including thousands of vitamin D deficient patients (NCT03096314 and NCT03188796) will provide more knowledge soon. VIOLET randomised patients with 25hydroxyvitamin D levels below 20 ng/ml "at risk for ARDS" to a single high dose of vitamin D3 (540,000 IU) and evaluated its effect on the primary outcome 90-day-mortality. It was prematurely stopped in 2018, and no results have yet been published.

VITDALIZE is a European multicentre RCT including severely vitamin D deficient patients in the ICU with a 25-hydroxyvitamin D level < 12 ng/ml and randomises patients to a loading dose of vitamin D3 (540,000 IU) followed by 4000 IU daily for 90 days – the primary outcome is 28-day-mortality. Currently, more than 20 sites in Austria (PI: K. Amrein) and Belgium (PI: J.Ch. Preiser) are active and recruitment will continue for the next few years.

In conclusion, vitamin D deficiency is highly prevalent and associated with adverse outcomes worldwide in paediatric and adult critically ill patients. Moreover, it appears reasonable that vitamin D deficiency is an important contributor to adverse outcomes during and following acute illness. If so, vitamin D's overall effect may be small, but even a tiny effect of an inexpensive treatment, on important clinical outcomes, with a very low rate of side effects, may prove to be a game changer in intensive care some day. ■

Key points

- Vitamin D has the potential to represent an independent, modifiable risk factor amendable to rapid normalisation through loading dose supplementation.
- Vitamin D deficiency is associated with an increased risk of mortality, organ dysfunction, infections, prolonged ICU and hospital stay as well as increased duration of mechanical ventilation.
- Preoperative malnutrition, poor general health, limited sunlight exposure, and preexisting liver and kidney dysfunction are primary causes of vitamin D deficiency.
- High dose vitamin D supplementation is safe and cost-effective in critically ill patients.
- Vitamin D shows immunomodulating, organ protective and bone health promoting properties in high risk cardiac surgery and transplant patients

References

Al-Tarrah K, Hewison M, Moiemen N, Lord JM (2018) Vitamin D status and its influence on outcomes following major burn injury and critical illness. Burns & trauma, 6:11.

Amrein K, Papinutti A, Mathew E, Vila G, Parekh D (2018) Vitamin D and critical illness: what endocrinology can learn from intensive care and vice versa. Endocrine connections, 7(12):R304-r15.

Amrein K, Zajic P, Schnedl C, Waltensdorfer A, Fruhwald S, Holl A, et al. (2014a) Vitamin D status and its association with season, hospital and sepsis mortality in critical illness. Critical care, 18(2):R47.

Amrein K, Schnedl C, Holl A, Riedl R, Christopher KB, Pachler C et al. (2014b) Effect of high-dose vitamin D3 on hospital length of stay in critically ill patients with vitamin D deficiency: the VITdAL-ICU randomized clinical trial. JAMA, 312(15):1520-30.

de Haan K, Groeneveld AB, de Geus HR, Egal M, Struijs A (2014) Vitamin D deficiency as a risk factor for infection, sepsis and mortality in the critically ill: systematic review and meta-analysis. Critical care, 18(6):660.

Herman CR, Buth KJ, Legare JF, Levy AR, Baskett R (2013) Development of a predictive model for major adverse cardiac events in a coronary artery bypass and valve population. J Cardiothorac Surg, 8:177.

Leclair TR, Zakai N, Bunn JY, Gianni M, Heyland DK, Ardren SS et al. (2019) Vitamin D Supplementation in Mechanically Ventilated Patients in the Medical Intensive Care Unit. JPEN Journal of parenteral and enteral nutrition.

Manson JE, Cook NR, Lee IM, Christen W, Bassuk SS, Mora S et al. (2019) Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease. The New England journal of medicine, 380(1):33-44.

Ney J, Heyland DK, Amrein K, Marx G, Grottke O, Choudrakis M, et al. (2018) The relevance of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D concentration for postoperative infections and postoperative organ dysfunctions in cardiac surgery patients: The eVIDenCe study. Clin Nutr.

Ramos-Martinez E, Lopez-Vancell MR, Fernandez de Cordova-Aguirre JC, Rojas-Serrano J, Chavarria A, Velasco-Medina A et al. (2018) Reduction of respiratory infections in asthma patients supplemented with vitamin D is related to increased serum IL-10 and IFNgamma levels and cathelicidin expression. Cytokine, 108:239-46.

Sassi F, Tamone C, D'Amelio P (2018) Vitamin D: Nutrient, Hormone, and Immunomodulator. Nutrients, 10(11).

Thiem U, Olbramski B, Borchhardt K (2013) Calcidiol deficiency in end-stage organ failure and after solid organ transplantation: status quo. Nutrients, ;5(7):2352-71.

Turan A, Grady M, You J, Mascha EJ, Keeyapaj W, Komatsu R, et al. (2013) Low vitamin D concentration is not associated with increased mortality and morbidity after cardiac surgery. PloS one, 8(5):e63831.

Zittermann A, Kuhn J, Ernst JB, Becker T, Larisch J, Dreier J, et al. (2016) Circulating 25-Hydroxyvitamin D and 1,25-Dihydroxyvitamin D Concentrations and Postoperative Infections in Cardiac Surgical Patients: The CALCITOP-Study. PloS one, 11(6):e0158532.

Zittermann A, Kuhn J, Dreier J, Knabbe C, Gummert JF, Borgermann J (2013) Vitamin D status and the risk of major adverse cardiac and cerebrovascular events in cardiac surgery. Eur Heart J, 34(18):1358-64.

Julie Darbyshire
Critical Care Research Programme Manager
Nuffield Department of Clinical Neurosciences
University of Oxford

@JLDarbyshire

Julie.Darbyshire@ndcn.ox.ac.uk

Noise in the intensive care unit: where does it come from and what can you do about it?

Practical measures and interventions to reduce noise levels in the ICU and to improve the patient experience.

The intensive care unit (ICU) is known to be noisy and is getting louder (Busch-Vishniac et al. 2007). Despite several trials, no interventions have been able to reduce noise levels by a meaningful amount (Li et al. 2011; Boyko et al. 2017; Johansson et al. 2017). There tends to be a view that high noise levels are to be expected in the ICU due to the level of care being delivered, and that little can be done to change this (Litton 2019). However, our recent study (SILENCE: NIHR Research for Patient Benefit ref: PB-PG-0613-31034) suggests that sound levels can be lowered if staff can be encouraged to think differently about the problem and given the opportunity to be involved in designing interventions to reduce noise levels.

We used a mixed methods approach (Cresswell 2014) to assess the ICU environment. This involved qualitative analysis of both patient and staff experiences, and quantitative measurement of the ICU soundscape. Patients consistently reported that they were frequently disturbed, unable to sleep, frightened by the unfamiliar surroundings, and, after discharge, they struggled to reconcile their memories with reports of what had happened to them (Darbyshire et al. 2016). Ethnographic observations identified that the environment is somewhat chaotic, and generally organised for the convenience of staff. Nurses strived to deliver care efficiently, but it was apparent that there were discrepancies between 'work as imagined' (staff perception of working practice) and 'work as done' (the realities in the workplace) (Hollnagel 2016).

We also noticed that these frequent patient interactions contributed to noise and disturbance over and above the sounds directly associated with the task. Alarms, frequently triggered by the staff intervention, were left to run until care activities were completed. This behaviour contrasted with staff reports that they always silenced alarms immediately. It was clearly considered 'normal' to allow alarms in these circumstances. Acceptance of practice that would be considered inappropriate in other settings is an example of 'normalised deviance,' a term coined by Diane Vaughan in relation to the NASA Challenger disaster (Price and Williams 2018). When deviance occurs, it is common for actions and behaviours to be defended as necessary and justified. In this case, it might be that the patient needs to be rolled and the alarm is triggered due to physical movement rather than physiological abnormality. Staff therefore correctly recognised that these alerts were false-alarms, but did not obviously consider their contribution to local noise pollution, or the potential effects of this on patients.

> "almost 90% of alarms are unnecessary; staff (perhaps understandably) employ the precautionary principle and are reluctant to alter alarm volumes or patterns"

Mismatches between staff perception and reality are particularly important when thinking about culture change because if interventions focus on 'work as imagined,' the realities of 'work as done' are not addressed. Equally, addressing work as done without overt reference to how this differs from 'work as imagined' is likely to have limited effect as staff may not recognise the need for change.

Quantitative measurement of overall Sound Pressure Levels (SPL) was revealing, and supported the qualitative reports generated from patient interviews. It demonstrated SPL levels persistently higher than the World Health Organization (WHO) recommendations, with peak values frequently measured over 100dB (Darbyshire and Young 2013). Patterns were observed in the data. Handover periods were consistently one of the louder periods of a shift, and it was obviously quieter overnight, although still well above WHO guideline levels. We also found that simple environmental modifications can facilitate noise reduction strategies. We saw a number of "solutions" to noise problems; for example, wadding placed in a doorway to prevent the door slamming because the soft-close mechanism was broken and the lifting of trolleys in motion to prevent the sound of a squeaky wheel. We particularly noticed that nightshifts were quieter when lights were off except to facilitate care interventions. Darkness, therefore, seemed to be an indicator to staff that patients should be sleeping and that general activity levels should be low. We also noticed that whilst it seemed to be common to turn overhead lights out overnight for patients who were

not sedated, they were often left on above-sedated patients, thus contributing to the disruption of the circadian regulatory system (Bedrosian and Nelson 2017).

After compiling noise data and the qualitative results, an intervention strategy was designed using the principles of experience-based co-design [EBCD] (Locock et al. 2014). Simple solutions such as replacing broken metal bins with soft-close-lid plastic versions removed a key source of noise. The research group also liaised with local staff to write alarm management guidelines, incorporating individualised alerting parameters and suggesting that volume levels should be guided by changing ambient sound levels rather than simply being set to the maximum throughout the shift. We highlighted the lighting effect on night time noise to encourage better day/night differentiation and recommended that switching off main unit lights should become part of policy (Darbyshire and Hinton 2018). Finally, the research team engaged with a medical educationalist to design a teaching module comprising an e-learning package and a simulation exercise (Darbyshire et al. 2018). The experiential aspect of the immersive simulation contextualises the need to reduce noise levels in the ICU, as staff members are given the opportunity to experience the ICU from the patient's point of view. The course evaluation indicated this teaching is overwhelmingly effective at recreating the feelings reported by real ICU patients. The session could be stopped at any time by the participant, although none did so. After just a few minutes, staff reported feeling uncomfortable, confused, stressed, frightened, and alone; feelings which map closely to how patients describe their time in the ICU. In line with adult education theory (Kolb and Fry 1975), participants were encouraged to reflect on their experience and relate it to their patients who have no control over their situation, and who cannot take 'time out.'

One aspect of the simulation experience was to demonstrate the patient experience of alarms. As staff were healthy volunteers, the monitors were manipulated to sound an alarm tone while the participant was connected to it. This unexpected alarm was intended to simulate the concern that patients spoke about when they heard alarms. The disturbance caused by a noise such as an alarm is more than a simple function of volume. The intrusiveness of noise is dependent on its frequency. By design, alarms have similar sound qualities to a baby's cry or a human scream, representing primal triggers of attention in most humans. They are intended to be disturbing so that they attract attention. In open plan ICUs, this means that every alarm can be attended to by any member of staff. It also means that every alarm is heard by every patient. Even where patients are admitted to single rooms, they will be repeatedly disturbed by their own alarms.

> **"meaningful change is more likely with a wider understanding of the types of noise that are likely to be most disturbing, and better awareness of the consequences for patients of this constant disturbance"**

'Loudness' is a measure of sound that allows the subjective perception of the sound to be quantified (ISO 2017). Sounds of a higher pitch, such as alarms, are more likely to be disturbing. In our study, loudness levels showed a clear reduction of about 4dB between 1am – 4am, although this marked dip is not seen in the average decibel level which remains fairly constant (Darbyshire et al. 2019). This suggests that there were fewer alarm sounds during this period.

Implementing alarm management guidelines was challenging. While it has been reported that almost 90% of alarms are unnecessary (Gorges et al. 2009), staff (perhaps understandably) employ the precautionary principle (UN 1992) and are reluctant to alter alarm volumes or patterns. From a psychological perspective, however, this is an overly simplistic approach as auditory and visual distractors have a measurable impact on task performance (Simons 2000; Bressan and Pizzighello 2008; Molloy et al. 2015), and alarm fatigue is a well-recognised source of risk (Ross 2015; ECRI Institute 2011). Improvements then can be achieved in both patient comfort and safety through better understanding and use of alarms. Specifically, meaningful change is more likely with a wider understanding of the types of noise that are likely to be most disturbing, and better awareness of the consequences for patients of this constant disturbance.

SPL in Oxford were reduced by approximately 4dB in the four months after environmental changes were introduced, and after initial delivery of the teaching sessions.

Table 1. World Health Organization noise level recommendations

- Average patient room noise should remain at 30dB
- Below 30dB, no effects on sleep are observed except for a minor increase in the frequency of body movements.
- Below 40 dB, no evidence was found that the biological effects on patients was harmful to health.
- Noise level above 40 dB resulted in sleep disturbance, environmental insomnia, and increased use of somnifacient drugs and sedatives. Vulnerable groups may be more affected.
- Noise level above 55 dB is considered dangerous for patient health. Patients may be annoyed due to lack of proper sleep and the risk of cardiovascular disease may also increase.

Source: Night noise guidelines for Europe (2009). World Health Organization

The final phase of the SILENCE project was to design a system to report sound levels and feed this back in real time. The research team consulted with clinical staff throughout this development period. By the end of the SILENCE project, SPL had reduced a further 7dB to ~46dB (Young et al. 2018). This drop of 11dB is a significant change, that is easily noticeable in the environment.

A recent meta-analysis of interventions limiting patient exposure to noise and disturbance through the use of earplugs and eye masks has been shown to reduce the risk of delirium (Litton et al. 2016). It is highly likely that ambient noise levels also have a significant environmental effect on sleep. SILENCE and other similar studies have consistently reported the difficulties with measuring the duration/quality of sleep in the ICU (Jeffs and Darbyshire 2017; Bourne et al. 2007; Beecroft et al. 2008; van der Kooi et al. 2012). Better measures of sleep are therefore needed for routine clinical use if we are to be able to measure the effects of changing noise levels more accurately. Future research will need to focus on patient-oriented outcomes such as sleep and delirium, and their correlation with measures of sound.

We speculate that 'making a lot of noise about SILENCE' (without explicitly dictating behavioural change), may have contributed indirectly to the local improvements in loudness and SPL, essentially by activating what is commonly termed the "Hawthorne Effect." Encouraging staff to be directly involved with practical measures to improve the patient experience of ICU having been through a visceral experience of their own (thus having a personal understanding of the problem of noise in the ICU) seems to have been the key driver for change. In conclusion, mixed methods enable richer interpretation and deeper understanding than is possible through quantitative or qualitative methods alone. Focusing on patient experiences and including those working in the environment to help design change seems key to achieving significant success. ■

"auditory and visual distractors have a measurable impact on task performance, and alarm fatigue is a well-recognised source of risk"

Key points

- Sound levels in the intensive care unit can be reduced
- It is important to consider the quality of the sound as well as the volume
- Including patients and care delivery staff in the development of interventions changes group dynamic and improves engagement
- Immersive, experiential simulation teaching is a powerful learning tool
- Educational interventions need to align with adult educational theory

References

Bedrosian TA, Nelson RJ (2017) Timing of light exposure affects mood and brain circuits. Translational Psychiatry, 7, E1017.

Beecroft, JM., Ward M, Younes M, Crombach S, Smith O, Hanly PJ (2008) Sleep Monitoring in the intensive care unit: comparison of nurse assessment, actigraphy, and polysomnography. Intensive Care Med, 34: 2076-83.

Bourne RS, Minelli C, Mills GH, Kandler R. (2007) Clinical review: sleep measurement in critical care patients: research and clinical implications. Crit Care, 11: 226.

Boyko Y, Jennum P, Nikolic M, Holst R, Oerding H, Toft P (2017) Sleep in Intensive care unit: the role of environment. Journal Of Critical Care, 37: 99-105.

Bressan, P. & Pizzighello, S. 2008. The attentional cost of inattentional blindness. Cognition, 106, 370-383.

Busch-Vishniac I, West JE, Kwon P, Dunn J (2007) The challenges of noise control In hospitals. 14th international conference on sound and vibration. Cairns, Australia.

Cresswell JW (2014) Research design: qualitative, quantitative, and mixed methods Approaches. Los Angeles, London, New Delhi, Singapore, And Washington Dc, Sage Publications.

Darbyshire JL, Greig PR, Vollam S, Young JD, Hinton L (2016) "I Can Remember Sort of Vivid People...but to Me They Were Plasticine." Delusions on the Intensive Care Unit: What Do Patients Think Is Going On?. PLOS ONE, 11(7).

Darbyshire J, Young J, Bedford J, Redfern O, Hatch R. (2019) Understanding sound Pressure levels in the intensive care unit. 39th International Congress Of Intensive Care And Emergency Medicine, 19-22 March. Brussels.

Darbyshire JL, Hinton L (2018) Using patient narratives to design an intervention to Reduce noise in the intensive care unit. The Journal Of Health Design, 3(2): 109–112.

Darbyshire JL, Hinton L, Young J, Greig P (2018) Using the experience-based co-Design method to design a teaching package. Medical Education, 52: 1198.

Darbyshire JL, Young JD (2013) An investigation of sound levels on intensive care Units with reference to the WHO guidelines. Crit Care, 17, R187.

ECRI Institute (2011) Top 10 health technology hazards for 2012. Health Devices, 40: 1-18.

Gorges M, Markewitz BA, Westenskow DR (2009) Improving alarm performance in The medical intensive care unit using delays and clinical context. Anesth Analg, 108: 1546-52.

Hollnagel E (2016) The nitty-gritty of human factors. In: Shorrock, S. & Williams, C. (Eds.) Human factors and ergonomics in practice: improving system performance and Human well-being in the real world. Boca Raton, Fl: CRC Press.

ISO 2017. ISO 532-1-2017: Acoustics - methods for calculating loudness - Part 1: Zwicker Method.

Jeffs EL, Darbyshire JL (2017) Measuring sleep in the intensive care unit: a critical Appraisal of the use of subjective methods. J Intensive Care Med, 885066617712197.

Johansson L, Lindahl B, Knutsson S, Ogren M, Persson WK, Ringdal M (2017) Evaluation of a sound environment intervention in an ICU: A feasibility study. Aust Crit Care.

Kolb DA, Fry R (1975) Toward an Applied Theory of Experiential Learning. In: Cooper C. (Ed.) Theories Of Group Process. London: John Wiley.

Li SY, Wang TJ, Vivienne Wu SF, Liang, SY, Tung HH (2011) Efficacy of controlling night-time noise and activities to improve patients' sleep quality in a surgical intensive care unit. J Clin Nurs, 20: 396-407.

Litton E (2019) Let us apply early goal-directed sleep. 39th International Symposium On Intensive Care and Emergency Medicine, 19-22 March, Brussels.

Litton E, Carnegie V, Elliott R, Webb SA (2016). The efficacy of earplugs as a sleep hygiene strategy for reducing delirium in the ICU: A systematic review and meta-analysis. Crit Care Med.

Locock L, Robert G., Boaz A, Vougiou-kalou S, Shuldham C, Fielden J, Ziebland S, Gager M, Tollyfield R Pearcey J (2014) Using a national archive of patient experience narratives to promote local patient-centered quality improvement: an ethnographic process evaluation of 'accelerated' experience-based co-design. Journal Of Health Services Research & Policy, 19: 200-207.

Molloy K, Griffiths TD, Chait M, Lavie N (2015) Inattentional deafness: visual load Leads to time-specific suppression of auditory evoked responses. J Neurosci, 35, 16046-54.

Price M, Williams T (2018) When doing wrong feels so right: normalization of deviance. Journal Of Patient Safety, 14: 1-2.

Ross J (2015) Alarm fatigue: are you tuning out? Journal Of Perianesthesia Nursing, 30: 351-353.

Simons DJ (2000) Attentional capture and inattentional blindness. Trends In Cognitive Sciences, 4, 147-155.

UN 1992. Rio declaration on environment and development, ISBN: 9 21 100509 4.

Van Der Kooi AW, Leijten FS, Van Der Wekken RJ, Slooter AJ (2012) What are the opportunities for EEG-based monitoring of delirium in the ICU? J Neuropsychiatry Clin Neurosci, 24: 472-7.

Young J, Darbyshire J, Hinton L (2018) Sleep in the ICU: Limiting elements of noise in the critical care environment (SILENCE). A feasibility study (NIHR RfPB Ref: PB-PG-0613-31034 Final Project Report. NIHR

Focus Meeting
on Perioperative Medicine
Mother and Child 2019

15 - 16 OCTOBER

ROME

ITALY

esahq.org

Mark P. Abrams
Director, Patient Engagement
Heartbeat Health
New York, NY, USA

mark@heartbeathealth.com

www.heartbeathealth.com/

@mpabrams

Keeping the Person in Personalised Medicine

As Personalised Medicine endeavours to discover more specific aetiologies and treatments of disease based on genetics and basic science research, it is crucial to maintain a focus on the patient-doctor relationship in order to more fully optimise patient care.

In a world where the cutting edge is a crowded place, and people's lives are at stake, healthcare is an industry where growth is happening inward rather than outward. Solutions are being discovered by diving deeper into issues rather than spreading more broadly. Personalised Medicine, also referred to as Precision Medicine, is the science of making care better by being more specific in assessments, diagnostics, and treatments. Its defining feature is innovating on the very basis of what makes each person unique down to their genetic core. Yet, as medical research and technology improve our ability to learn about patients along with what makes them healthy, what causes disease, and what treatments might be more effective, it may be ignoring what patients often yearn for - the age-old therapeutic patient-doctor relationship.

In medical education, there is a distinction made to differentiate between the words illness and disease. A disease is a pathological state that is diagnosed through history-taking, physical examination, and testing. It can often be treated, ameliorated, and even cured by various means. An illness is a much broader term that is defined by a person's experience in having a diagnosis. It encompasses not only the impact of the disease, but their personal journey through obtaining that diagnosis, the associated symptoms, the treatment, and the after-effects. It is taught that while medication or other therapy may cure a disease, what makes the patient-doctor relationship so special is the ability - the privilege - of treating the whole patient's illness. This concept is what may be at least partially lost when the medical community seeks finite answers to more complex issues.

Although one might think that being able to produce such definitive information such as could be provided by cracking the entirety of the wealth of information that the genetic code offers would make the art of medicine obsolete in favour of hard science that can prevent and/or cure all, this is not necessarily the case. An example of this has been researched using allergic responses. The pathophysiologic mechanism of an allergic response has been well-delineated along with excellent, specific therapeutic targets to prevent it. In this study, patients received a skin prick containing histamine, which causes a type of allergic response, and their symptoms of itchiness and irritation were measured. Approximately half of the patients were told by the doctor after three minutes that their symptoms would start to improve and the other half were not. The researchers examined how this simple comment of reassurance affected patients' perception of discomfort from the skin prick. They found that although physiologically this comment should not affect the histamine reaction occurring in the skin, patients who were reassured had significantly improved symptoms after hearing that comment compared to those who did not get any reassurance (Leibowitz et al. 2018). What this infers is that the patient-doctor relationship is in itself therapeutic. The idea that if a patient thinks something will help them, it actually does help, is known as the placebo effect. It is widely shown in various areas of research to be more effective than nothing, yet its ability to have these pleiotropic effects remains mysterious.

> **"Personalised Medicine has emerged as a means to take the field of medicine to the next level"**

Personalised Medicine has emerged as a means to take the field of medicine to the next level. The National Institutes of Health (NIH) has led a nationwide initiative in the United States called All of Us, which is a research programme seeking to collect genetic data on at least one million Americans from diverse backgrounds in both healthy and diseased states in order to help answer questions facing the medical community. With enough data, the hope is to be able to discover a genetic basis for why certain people develop certain diseases and help identify which people that have diseases might have specific therapeutic targets available to them.

Better yet, this information could ultimately help determine which diseases could be prevented altogether. In 2016, the NIH committed $200 million to this (About the All of Us Research Program 2019).

Certainly, doctors and patients would agree that better solutions to the health problems facing people - some largely preventable at epidemic proportions such as heart disease - are desperately needed. Medical research, in particular, the application of technology, likely has the power to solve many of these complex questions in due time. Through Personalised Medicine initiatives, there may very well be definitive answers one day to questions about whether someone will get cancer or have a heart attack. Doctors, or even computer algorithms, might be able to recommend medications for diseases based on genetic mutations that cause disease. However, as answers to questions

> **“in order to fully help people, we must not only try to cure disease, but treat patients, and maintain humanism in medicine”**

about the health of patients becomes more precise, doctors must realise that in order to fully help people, we must not only try to cure disease, but also remember to treat patients, positively affect their illnesses, and maintain humanism in medicine. We must remember that helpful answers are not only found by looking deeper, but also by looking to the patient. ■

Conflict of Interest
Mark P. Abrams has declared no conflict of interest.

Key points

- Personalised Medicine, also known as Precision Medicine, is an initiative to discover the basic science and genetic basis of both healthy and disease states.
- While a disease is a name for a diagnosis, illness is a term that encompasses a person's experience of symptoms, diagnosis, treatment, and living with a disease.
- The patient-doctor relationship has been shown to influence the effectiveness of different medical treatments, possibly related to the placebo effect.
- While evidence-based treatments emanating from Personalised Medicine may offer hope for better health outcomes, patients also benefit from the relationship they have with their doctor.

European guidelines on the management of traumatic induced bleeding

Interview with Rolf Rossaint, Prof. of Anaesthesiology, RWTH University Aachen, Germany.

Rolf Rossaint is a Professor and Chairman of the Department of Anaesthesiology of the University Hospital at the RWTH University Aachen, Germany. Prof. Rossaint has published several high-quality studies dealing with the treatment of severe acute respiratory distress syndrome (ARDS). He has also been actively involved in research on the pathophysiology of trauma associated coagulopathy and possible treatments. A group of international experts involved in this research is chaired by Prof. Rossaint. The group has recently published the updated European guidelines on the management of traumatic induced bleeding. Prof. Rossaint discusses these new guidelines with ICU Management & Practice.

You chair an international group of experts involved in conducting research on the pathophysiology of trauma associated with coagulopathy and possible treatments. What are the goals of this group?

The ultimate goal of this group is to improve survival in trauma patients. Back in 2004, when we founded the international expert group on advanced bleeding control for trauma (ABC-T), we realised that the knowledge about the occurrence and specific pathophysiology of trauma induced coagulopathy could be improved. Moreover, we found that there was not an evidence-based approach or standard to treat the bleeding in major trauma.

Severe traumatic injury and post-traumatic bleeding is a leading cause of death among injured patients. These patients often develop multiple organ failure and die more frequently compared to patients with similar injuries in the absence of coagulopathy. Why do you think that is?

The early acute coagulopathy associated with traumatic injury has recently been recognised as a multifactorial primary condition that results from a combination of bleeding-induced shock, tissue injury-related thrombomodulin upregulation, thrombin-thrombomodulin-complex generation and the activation of anticoagulant and fibrinolytic pathways. This pathophysiology seems to promote multiple organ failure.

The European clinical practice guidelines are part of the European STOP the Bleeding Campaign. Can you tell us about this campaign?

The STOP the Bleeding Campaign was launched in 2013 and aims to increase awareness of the phenomenon of post-traumatic coagulopathy and its appropriate management by publishing European guidelines for the management of the bleeding trauma patient, by promoting and monitoring the implementation of these guidelines and by preparing promotional and educational material, organising activities and developing health quality management tools. The campaign aims to reduce the number of patients who die within 24 hours after arrival in the hospital due to exsanguination by a minimum of 20% within the next 5 years.

The acronym **STOP** comprises the following elements:

Search for patients at risk of coagulopathic bleeding,

Treat bleeding and coagulopathy as soon as they develop;

Observe the response to interventions;

Prevent secondary bleeding and coagulopathy

Are there any major changes in the fifth edition of the European guideline on management of major bleeding and coagulopathy compared to the fourth edition?

Advances in our understanding of the pathophysiology of post-traumatic coagulopathy have supported improved management strategies, including evidence that early, individualised goal-directed treatment improves the outcome of severely injured patients. Therefore, in the fifth edition, we pronounce the importance of goal-directed treatment after an initial empiric starting phase.

Moreover, the overall organisation of the current guideline has been designed to reflect the clinical decision-making process along the patient pathway in an approximate temporal sequence. Recommendations are grouped

behind the rationale for key decision points, which are patient- or problem-oriented rather than related to specific treatment modalities.

In addition, while these recommendations provide guidance for the diagnosis and treatment of major bleeding and coagulopathy, emerging evidence supports the author group's belief that the greatest outcome improvement can be achieved through education and the establishment of and adherence to local clinical management algorithms.

A key recommendation in the guidelines is to transport patients quickly to a trauma facility and to minimise the time between injury and bleeding control. Keeping in mind the fact that there is significant variation in trauma care systems within different hospital networks, a particular region and across different countries, what measures do you think can be taken to ensure this happens?

The main point is to create the awareness of the paramedics and prehospital emergency physicians that it is important and sometimes life-determining to minimise the time between injury and bleeding control. However, equally important is that the patient is transferred to this trauma centre which is able to treat the patient appropriately, even if the transfer to the hospital is a little bit longer than to the next hospital.

There is a new recommendation in the fifth edition related to the initial management of patients with expected massive haemorrhage with fresh frozen plasma (FFP). Can you elaborate on that?

In the initial management of patients with expected massive haemorrhage, we recommend one of the two following strategies:

- FFP or pathogen-inactivated FFP in a FFP:RBC ratio of at least 1:2 as needed. (Grade 1C)
- Fibrinogen concentrate and RBC. (Grade 1C)

Since neither of the two strategies has been shown to be better than the other, we recommend both possibilities. However, we have to be aware that with fresh frozen plasma, a severe fibrinogen deficiency cannot be corrected.

There is no doubt that these guidelines are very comprehensive. But in your opinion, how closely are these guidelines adhered to in actual clinical practice?

The overall organisation of the current guideline has been designed to reflect the clinical decision-making process along the patient pathway in an approximate temporal sequence. Therefore, I believe that the guideline is closely adhered to the actual clinical practice. Moreover, since the recommendations are grouped patient- or problem-oriented, it is easy to translate them into clinical practice.

> "in the fifth edition of the European guideline on management of major bleeding and coagulopathy, we pronounce the importance of goal-directed treatment after an initial empiric starting phase"

What measures do you think can be implemented to ensure greater adherence to these guidelines?

We know that adherence to these European guidelines on the management of bleeding trauma patients resulted in higher patient survival. The implementation of our recommendations might be facilitated by a checklist approach analogous to the Safe Surgery Initiative, which led to fewer postoperative complications. In addition or alternatively, it may be possible to implement our recommendations using "bundles," as has been successfully achieved during the implementation of the Surviving Sepsis Campaign guidelines. Suggested items that should be included in such a checklist or in such bundles as listed in our guideline.

Overall, how feasible do you think correction of trauma-induced coagulopathy is in severely injured patients?

We know that about 25% of all severe and bleeding trauma patients are arriving in our hospital with a trauma induced coagulopathy. My guess would be that we are able to correct the severe coagulopathy in about 50% in the following hours if we follow all the recommendations. In some of our patients, the trauma induced coagulopathy will last for much longer. A damage control surgery approach is demanded. During the intensive care treatment, the trauma induced coagulopathy will resolve.

You have significant expertise in the treatment of severe acute respiratory distress syndrome (ARDS). Are there any future research areas or projects you are working on related to treatment strategies for patients with moderate and severe ARDS?

At present, I am leading a basic German Research Foundation research programme entitled "Towards an implantable lung" (SPP 2014). Here, we are searching for new approaches to overcome the problem in the coagulation cascade during extracorporeal lung support, which is often used in the most severe ARDS patients.

You have been involved in investigating the cardio and neuroprotective effects of Xenon? Can you tell us something about this experimental work?

Indeed, we did a lot of research in this area. Although we were able to demonstrate the cardio- and neuroprotective effects in many research projects and different species, so far, we could not demonstrate a morbidity or mortality reduction in patients.

You are also interested in the use of e-health in prehospital emergency medicine. What role do you think e-health will play in future in intensive care and emergency medicine?

Yes, I established the worldwide first holistic prehospital tele-emergency system in Aachen. Since five years, it is routinely used as a structural addition to the conventional physician-based prehospital emergency system. So far, we treated about 15.000 patients using prehospital emergency telemedicine without system-related complication. I am quite sure that telemedicine in prehospital emergencies and in intensive care will play an important role to allow for a timely and guideline-based diagnosis and therapy. ■

SPAIN I BARCELONA

30 May - 01 June

Euroanaesthesia 2020

THE EUROPEAN ANAESTHESIOLOGY CONGRESS

esahq.org

Highlights from the I-I-I Blog (I expert, I question, I answer)

A selection from the ICU Management & Practice I-I-I blog. Have you got something to say?

Visit https://healthmanagement.org/c/icu/list/blog or contact editorial@icu-management.org

Peter Pronovost

Chief Clinical Transformation Officer - University Hospitals, Cleveland, Ohio

@PeterPronovost

What should the intensivist of the future look like?

"The intensivist of the future will need three sets of principles that guide everything they do: an internal set, an interpersonal set and an organisational set. Those internal principles that we should be selecting for are people who are humble, curious and compassionate. The second set of principles is to respect, appreciate and help others. The third set of behaviours is also key yet underdeveloped in healthcare. They are to be accountable to continuously improve myself, my organisation and my community."

See more: https://healthmanagement.org/c/icu/post/what-should-the-intensivist-of-the-future-look-like

Ruth Kleinpell

Director - Center for Clinical Research & Scholarship, Rush University Medical Center

@RKleinpell

Vicki Good

Vice President Quality/Safety - Mercy Hospital Springfield Communities, Springfield, Missouri

Burnout syndome in critical care: what needs to happen now?

"One of the first things ICU leaders must do is learn how to recognise when staff is experiencing burnout syndrome. Once recognised, interventions should begin. Interventions should be based on the individual as burnout is not "equal" across everyone. One person's burnout may be related to lack of rest from the stressful environment, therefore a vacation or not working overtime might address those concerns. Another person's experience may be related to feeling a lack of professional/personal accomplishment. This individual might respond to projects, going back to school or engaging with a professional association."

See more: https://healthmanagement.org/c/icu/post/burnout-syndrome-in-critical-care-what-needs-to-happen-now

Nidhi Nikhanj

Assistant Medical Director - Banner Telehealth Services Phoenix, Arizona USA

Bedside Ultrasonography: Six success factors for implementation

"The Surviving Sepsis campaign's bundle of care practices for patients with severe sepsis or septic shock recommends bedside cardiovascular ultrasound as one of the recommended methods for evaluating volume status and tissue perfusion, with the scan to be performed with six hours of clinical presentation. Bedside echo has been shown to improve diagnostic accuracy, reduced time delays for procedures, superior accuracy in evaluating fluid status in heart failure patients, reduced cost for procedures, support for use of ultrasound as the 'third eye' to help the intensivist manage patients and assessment of shock to determine haemodynamic status, fluid resuscitation, and interventions."

See more: https://healthmanagement.org/c/icu/post/bedside-ultrasonography-6-success-factors-for-implementation

AGENDA

For a full listing of events visit https://iii.hm/swz

JUNE

1-3 Euroanaesthesia 2019
Vienna, Austria
https://iii.hm/uxm

3-4 6th World Congress and Exhibition on Antibiotics and Antibiotic Resistance
London, UK
https://iii.hm/uxn

6-8 ESICM LIVES Forum - AKI as a syndrome
Nice, France
https://iii.hm/uxo

8-11 42nd Annual Conference on Shock
Coronado, USA
https://iii.hm/uxp

10-11 Care Convention 2019 - Airway & Respiratory Conference
Coventry, UK
https://iii.hm/uxq

12-15 ICEM 2019
Seoul, South Korea
https://iii.hm/uxr

13-15 9th Europaediatrics
Dublin, Ireland
https://iii.hm/uxs

18-21 30th Annual Meeting of the European Society of Paediatric and Neonatal Intensive Care - ESPNIC 2019
Salzburg, Austria
https://iii.hm/uxt

20-21 Neurosciences in Intensive Care International Symposium (NICIS) 2019
Paris, France
https://iii.hm/uxu

AUGUST

31-3 2019 ESPEN - European Society of Clinical Nutrition and Metabolism Congress
Krakow, Poland
https://iii.hm/uxv

SEPTEMBER

11-14 European Society of Regional Anaesthesia (ESRA) Congress 2019
Bilbao, Spain
https://iii.hm/uxw

15-17 The Future of Intensive Care - A Brainstorming Meeting 2019
Nice, France
https://iii.hm/uxx

16-17 British Association of Critical Care Nurses (BACCN) Conference 2019
Edinburgh, Scotland
https://iii.hm/uxy

19-21 ESPA 2019 – 11th European Congress for Paediatric Anaesthesia
Rotterdam, Netherlands
https://iii.hm/uxz

19-21 European Resuscitation Council (ERC) Congress 2019
Ljubljana, Slovenia
https://iii.hm/uy0

19-22 EAP (European Academy of Paediatrics) 2019 Congress and MasterCourse
Porto, Portugal
https://iii.hm/uy1

28-2 ESICM LIVES 2019 - 32nd Annual Congress
Berlin, Germany
https://iii.hm/uy2

ICU
MANAGEMENT & PRACTICE

ICU MANAGEMENT AND PRACTICE IS PUBLISHED BY
MindByte Communications Ltd
9, Vassili Michailidi CY-3026 Limassol, Cyprus
Email — office@icu-management.org
Website — icu-management.org

SUBSCRIPTION RATES
One year — 55 Euros + 5% VAT if applicable
Two years — 90 Euros + 5% VAT if applicable
Note: For a free digital subscription please contact Samna Ghani, editorial@icu-management.org

PRODUCTION, PRINTING AND DISTRIBUTION
Printed in Hungary by ABEL Printing
Total classic and digital distribution: 21,500
ISSN = 1377-7564

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

ICU Management & Practice is independently audited by Top Pro CY.

CELEBRATING LIFE-CHANGING CREATIVITY

CANNES LIONS
INTERNATIONAL FESTIVAL OF CREATIVITY

THE 66TH INTERNATIONAL FESTIVAL OF CREATIVITY
17 - 18 JUNE 2019

BOOK NOW
CANNESLIONS.COM

PLEASE VISIT US AT BOOTH B0802

Factor concentrates
in the perioperative management of coagulopathy

Sunday 2 June 2019, 12:15–13:45
Room Cello, Messe Wien Congress Centre, Vienna, Austria

Programme

Chairs: Jens Meier (Austria), Christoph Schlimp (Austria)

12:15 Chairs' welcome

Pathophysiology of trauma and revised European trauma guidelines
Donat Spahn (Switzerland)

Coagulopathy during cardiac surgery: the role of factor concentrates
Marco Ranucci (Italy)

Treatment options for factor-Xa inhibitor-related bleeding
Jerrold Levy (USA)

Reversal agent use in patients treated with DOACs or vitamin K antagonists: results from the RADOA registry
Edelgard Lindhoff-Last (Germany)

Closing remarks

13:45 Close of symposium

Lunch will be provided

Satellite symposium at Euroanaesthesia 2019

CMD-BRX-0048
05/2019

CSL Behring