

Pulmonary and Critical Care Updates

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Robert A. Fowler¹, Neill K. J. Adhikari¹, Damon C. Scales¹, Warren L. Lee¹, and Gordon D. Rubenfeld¹

¹Interdepartmental Division of Critical Care Medicine, University of Toronto, Toronto, Ontario, Canada

CRITICAL CARE IN THE GLOBAL CONTEXT

Critical care comprises only one part of the continuum of medical care, which itself is only one determinant of population health. U.S. expenditures on health care were \$2.1 trillion in 2006 and accounted for 16% of the gross domestic product, of which 10% is estimated to be spent on critically ill patients (1). Despite this vast investment in medical care, the United States ranks poorly among Organization for Economic Cooperation and Development countries on many standard measures of health (2). In addition, access to health care in the United States is woefully incomplete—45 million citizens, and millions more immigrants, lack health insurance (2). Nearly 90 million Americans lacked health insurance for at least 1 month during 2006–2007 (3). Universal access to health care in the United States has been a prominent feature of the current U.S. electoral cycle and is receiving increasing attention in the medical literature.

Although access to available care in North America is imperfect, basic health care services in much of the developing world are seriously lacking. AIDS in sub-Saharan Africa accounts for 72% of global AIDS deaths, and average life expectancy in this geographic area is 47 years—three decades shorter than in North America or Europe (4). *Critical care* as we know it in developed countries may not be available in developing nations; however, we would certainly recognize many patients dying of AIDS, malaria, diarrheal illness, and malnutrition in hospital wards as *critically ill*. Simple resources taken for granted in an intensive care unit (ICU) in the developed world, such as electricity, oxygen, and safe transportation, are often unavailable (5).

Global inequities in health outcomes are not being ignored. The United Nations has set ambitious Millennium Development Goals to be reached by 2015 (6, 7). These investments are not entirely altruistic. Resistant transmissible pathogens, including HIV, pandemic influenza, severe respiratory syndrome, and tuberculosis, emerge from these regions and affect the developed world, as does the physical conflict that inevitably arises from human suffering. Such problems of the developing world can easily and rapidly become problems of the developed world.

The reflective clinician may be overwhelmed by the apparent irrelevance of much of critical care in the face of the enormity of global inequities in health outcomes. Critical care is not unique in this regard. From the perspective of global health, much of modern medical care, with the possible exceptions of antibiotics and vaccinations, probably suffers from the same comparisons. However, this does not excuse us from contribut-

ing where we can: donating time, knowledge, and resources; advocating for less expensive medication; and developing more feasible strategies to deliver intensive care in underserved areas (8).

PROMINENT STUDIES

Two randomized controlled trials (RCTs) suggested a role for corticosteroids in preventing extubation failure (9, 10). A large multicenter RCT enrolling immunocompetent adults at risk of ventilator-associated pneumonia found that there were no statistically significant differences in 28-day mortality, rate of targeted antibiotic therapy, or days alive without antibiotic use between either bronchoalveolar lavage- or endotracheal aspiration-based diagnostic strategies (11). An end-of-life communication strategy between health care professionals and relatives of critically ill patients increased discussion in family conferences and decreased post-traumatic stress, anxiety, and depression among relatives (12). A time-series analysis of an evidence-based intervention of central venous catheter insertion and care, applied to more than 100 ICUs, decreased the median rate of catheter-related bloodstream infections from 2.7 per 1,000 catheter-days to 0 (13). A vasopressor strategy of norepinephrine plus dobutamine found no clinically important differences in outcome compared with one using epinephrine in patients with septic shock (14). The Resolution of Organ Failure in Pediatric Patients with Severe Sepsis (RESOLVE) study of drotrecogin alfa versus placebo for children with severe sepsis found no differences in clinical outcomes (15). Although not addressing the efficacy of drotrecogin alfa, one trial demonstrated that continuing use of prophylactic heparin was safe in patients receiving drotrecogin alfa therapy and also suggested that stopping heparin in patients in this setting might actually be harmful (16). Epoetin alfa (40,000 U) administered weekly for a maximum of 3 weeks to critically ill patients resulted in more thrombotic events but not fewer red cell transfusions (17). In one of the largest pediatric RCTs ever conducted, use of a hemoglobin transfusion threshold of 7 g/dl decreased transfusion requirements without increasing adverse outcomes (18). *Post hoc* analysis of the Saline versus Albumin Fluid Evaluation (SAFE) study found higher mortality among patients with traumatic brain injury who received albumin as a resuscitation fluid (19). Finally, the growing body of literature failing to show improved outcomes with use of pulmonary artery catheters has resulted in stepwise reductions in their use over the past decade (20).

ACUTE LUNG INJURY AND MECHANICAL VENTILATION

Cellular and Molecular Mechanisms

Numerous studies attempted to elucidate the mechanism of acute lung injury (ALI) using animal models and, in particular, mice with targeted genetic deletions. Blocking platelet-neutrophil interactions reversed acid-induced lung injury in mice, a finding which the authors attributed, at least in part, to preventing an

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Correspondence and requests for reprints should be addressed to Robert A. Fowler, M.D.C.M., M.S., Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Room D478, Toronto, ON, Canada M4N 3M5. E-mail: rob.fowler@sunnybrook.ca

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injurious effect of platelet-derived thromboxane A₂ (21). A wide range of molecules, including possible therapeutic targets in ALI, were studied this year: for example, blocking molecules, such as the apoptotic signal Fas, heat shock protein 90, adenosine, the transcription factor Nrf2, elastolytic protease cathepsin S, phagocyte-produced catecholamines, and p21-activated kinase, were protective against ALI (22–27). Administration of molecules such as endogenous adenosine and the stomach peptide ghrelin also appeared to be protective in experimental ALI (28, 29). Rather than study specific molecules, one group of investigators evaluated how the entire proteome was affected by different mechanical ventilation strategies (30).

A few groups described gene or cell transfer approaches as potential therapies for acute respiratory distress syndrome (ARDS). Electroporating the subunits of Na⁺/K⁺ ATPase into the lungs of mice protected against endotoxin-induced lung injury and improved preexisting pulmonary edema (31). Stem cell therapy for ARDS is being actively explored by a number of research groups. Beneficial effects have been noted in animals with endotracheal and intravenous delivery of stem cells and may be augmented by using stem cells transfected with angiopoietin-1, an angiogenic and endothelium-protective factor (32–34).

A few investigators explored the mechanisms underlying epidemiologic observations about ARDS in humans. The association of alcohol abuse with increased levels of ARDS may be due to a shift in the glutathione redox potential in alveoli (35). The association of diabetes with lower rates of lung injury may be explained by a protective effect of leptin resistance (36).

Epidemiology and Outcomes

The validity of the American–European Consensus Conference definition for ALI, which does not specify the ventilator settings at which the chest radiograph and oxygenation are assessed, was critically evaluated in a study that showed patient classification was affected by ventilator settings (37). One study questioned whether trauma-associated ALI constituted a different syndrome based on its pattern of biomarkers (38). Contrary to their initial hypothesis, the ARDS Network (ARDSnet) investigators found that higher levels of urinary nitric oxide were associated with better outcomes and speculated that this may reflect a subset of patients with more intact endothelial function (39). A recent study evaluating the incidence and outcome of ALI in children younger than 16 years in eight of nine pediatric ICUs in Australia and New Zealand found a significant burden of disease and a mortality of 35% (40). Body weight did not appear to affect mortality in one large cohort of patients with ALI, but severely obese patients spent more time in hospital and were more likely to be discharged to a location other than home (41). An arterial blood gas may not be necessary to identify patients who meet criteria for ALI if a proposed algorithm using the SpO₂:FiO₂ ratio instead of the PaO₂:FiO₂ ratio is valid (42).

Transfusion-related ALI

Several studies evaluated transfusion-related ALI (TRALI). Important findings included the following: identification of plasma products, particularly those from female donors, and antigranulocyte antibodies as risk factors for TRALI; the importance of TRALI in burn patients; and the association of red cell transfusion with ICU-acquired ARDS (43–47).

ALI Treatment

Two studies demonstrated significant reductions in ALI by systematically limiting injurious exposure to harmful mechanical ventilation and blood transfusions to patients at risk (48, 49). Appropriate mechanical ventilation is still the only therapy de-

monstrated to reduce mortality in ALI; however, two studies suggest that the ARDSnet strategy may still lead to alveolar overdistention in some patients (50, 51). Among patients with “early focal ARDS” on computed tomography scan, patients managed with “stress index”-guided mechanical ventilation received lower tidal volumes and less positive end-expiratory pressure than the ARDSnet protocol recommended, and these patients had less systemic inflammation (51). One-third of patients managed according to the ARDS Network goals of 6 ml/kg predicted body weight and inspiratory plateau pressure of less than 30 cm H₂O had evidence of tidal hyperinflation and worse inflammation, suggesting that a plateau pressure target of less than 28 cm H₂O may be necessary to prevent ventilator-induced lung injury (50). As investigators prepare for clinical trials of high-frequency oscillation in adults, interesting preparatory work to identify optimal settings is proceeding (52). A meta-analysis evaluating the effects of inhaled nitric oxide in over 1,200 patients with ALI found no effect on mortality, a modest 13% improvement in PaO₂:FiO₂ ratio, no effect on pulmonary artery pressure, and a concerning increase in the risk of renal dysfunction (53). Noninvasive ventilation for ALI may be feasible in experienced hands; however, the effect on outcome is still unclear (54). A potential role for prolonged “low dose” corticosteroids (methylprednisolone 1 mg/kg/d tapered over 28 d) in early ALI showed improvements in the primary endpoints of lung injury score and C-reactive protein at Day 7. Interpretation of other outcomes in this study is challenging because of the 2:1 randomization allocation, early stopping rules, crossover, and chance differences between the groups favoring corticosteroids (55). Recruitment maneuvers were carefully explored in a small group of patients with ARDS by evaluating edema fluid and demonstrated that recruitment may improve edema fluid clearance in responders but may actually impair clearance in nonresponders to the maneuver (56).

Mechanical Ventilation and Liberation

Assist control ventilation may improve sleep in the ICU compared with low levels of pressure support, raising the possibility that sleep quality can be influenced by optimizing mechanical ventilation; however, the mechanism for this effect was not well described in the study (57). In an unblinded randomized trial that challenges routine care in many ICUs, investigators found that routine chest physiotherapy prolonged duration of mechanical ventilation by 4 days and did not prevent reintubation or the need for rescue interventions for hypoxemia (58). An interesting study showed that low levels of pressure support and positive end-expiratory pressure, but not FiO₂, can lower the rapid shallow breathing index during a spontaneous breathing trial (59). Tracheostomy was not an independent risk factor for deep sternal wound infection in cardiac surgery patients in a single-center cohort study (60), but the safety of tracheostomy care was questioned in a study that found significant knowledge gaps in the management of tracheostomy-related emergencies (61).

Long-Term Outcomes

Although studies of post-traumatic stress disorder and its symptoms are increasing in critical care, there is significant variation in the methodology used to identify patients; this may account for reported prevalence rates ranging from 0 to 64% (62). Studies of risk factors for post-traumatic stress disorder symptoms identified female sex, younger age, prolonged sedation, delusional memories, and previous psychiatric illness (63, 64). The outcomes of a large cohort of chronically critically ill patients receiving prolonged mechanical ventilation at selected long-term care hospitals demonstrated considerable variability in the patient

population and outcomes. Half were liberated from mechanical ventilation at the time of discharge; however, only 30% were known to be alive 1 year postadmission (65). Sexual dysfunction was common 3 to 8 years after the acute illness in a group of critically ill trauma patients and was associated with depression (66). A small study without a validation cohort explored the predictive value of combining clinical examination, neurophysiologic, and biomarkers to predict outcome after cardiac arrest (67).

INFECTION PREVENTION AND SEPSIS

Cellular and Molecular Mechanisms

Observations of cytokine and coagulation factors in patients with sepsis continue to yield interesting results. The hypothesis that the progression to sepsis is due to an imbalance between pro- and antiinflammatory cytokines could not be validated in a large, well-described cohort of patients with community-acquired pneumonia, which illuminated the heterogeneity of the cytokine response (68). Abnormalities in protein C and other coagulation parameters are associated with organ failure but may be independent of infection (69). A number of groups characterized the kinetics of high mobility group box 1 protein, a DNA binding protein released by macrophages and necrotic cells that acts as a potent proinflammatory stimulus, in patients with sepsis (70, 71).

Gene expression profiling was used to discover a biologic "signature" of sepsis and to identify novel mediators of the syndrome including the transcription factor *C/EBP δ* (72, 73). Novel and complex mechanisms of sepsis have been explored in a number of articles. Mrp8 and Mrp14, which are abundant cytosolic proteins in neutrophils and monocytes, act as endogenous ligands of Toll-like receptor 4; mice deficient in these proteins are protected against septic shock (74). Platelet interactions with neutrophils lead to neutrophil extracellular trap formation in the hepatic microvasculature, which ensnares circulating bacteria (75). Mice deficient in CD14 (part of the receptor complex for endotoxin from gram-negative bacteria) are protected against infection with the gram-positive *Streptococcus pneumoniae* (76). Nucleotide oligomerization domain (NOD) protein 1, a cytosolic protein that recognizes peptidoglycan from gram-negative bacteria, acts as an important mediator of septic shock (77). Nitric oxide may impair chemotaxis by down-regulating the chemokine receptor CXCR2 on the neutrophil surface (78). A study exploring a biologic explanation for sex-related differences in toxic shock outcome, demonstrated that female mice have increased production of and sensitivity to tumor necrosis factor- α when exposed to superantigen (79).

Several interesting narrative reviews of sepsis were published this year. This includes a description of the cholinergic antiinflammatory pathway, a review on agonists and antagonists of Toll-like receptors, and a thoughtful discussion of the differences between animal models of sepsis and the disease in humans (80–82).

Infection Prevention

Single rooms may prevent bloodstream infections and cross-transmission of pathogens in ICUs (83). Device use was found to be a major risk factor for developing ICU-acquired infections, but was not associated with mortality (84). A small RCT of *Lactobacillus rhamnosus* strain GG administered as a probiotic to critically ill children was stopped early because of lack of efficacy and concerns about safety (85). An endotracheal tube with an ultrathin polyurethane cuff designed to reduce fluid leakage, combined with subglottic secretion drainage, was associated with a threefold reduction in ventilator-associated pneumonia in

comparison to a conventional endotracheal tube (86). Selective decontamination of the digestive tract reduced infection rate due to gram-negative organisms, but not mortality, in an RCT involving patients with multiple trauma (87). A meta-analysis demonstrated reduced ventilator-associated pneumonia through the use of topical oral antibiotics and antiseptics (88). Daily cleansing of medical ICU patients with chlorhexidine cloths was associated with fewer bloodstream infections in one RCT (89). An educational campaign was successful in increasing hand hygiene recommendations (90).

Sepsis and Inflammatory States

The incidence of sepsis was 367 per 100,000 adult inpatients in Spanish hospitals, with severe sepsis in 104 per 100,000 inpatients. Only 32% of patients with severe sepsis received care in an ICU (91). A prospective observational study of patients with atherosclerotic disease found that those receiving statins were significantly less likely to have infection-related mortality (92). Reduced selenium levels are common in critically ill patients and are associated with worse outcomes (93). Two, probably underpowered, RCTs of selenium infusion in sepsis failed to show a statistically significant effect on mortality (94, 95).

Meta-analyses of intravenous immune globulin as an adjunctive therapy for sepsis or septic shock found a reduced risk of death for adults and children, but this association was attenuated when only high-quality RCTs were included (96, 97). The most recent large RCT did not find a mortality difference between intravenous immune globulin and placebo treatment among patients with score-defined severe sepsis (98). Italian and Canadian observational studies found drotrecogin alfa was commonly used off-label, was associated with bleeding in 10% of patients, and was possibly associated with a higher mortality rate when used for scheduled surgical patients who developed postoperative sepsis (99, 100).

A worldwide study of the incidence of community-acquired pneumonia showed that greater than 20% of cases were due to atypical pathogens, indicating that empiric antibiotics should be directed toward these organisms (101). A multicenter RCT of early versus delayed antibiotics for severe necrotizing pancreatitis demonstrated no statistically significant differences in clinical outcomes (102).

SUBSPECIALTY CRITICAL CARE

Cardiac Surgery

Several articles examined critical care of cardiac surgical patients. Using a cohort design with historical controls, investigators showed that a protocol incorporating end-diastolic volume index goals for hemodynamic therapy in patients undergoing cardiac surgery was associated with reduced need for vasopressors, catecholamines, mechanical ventilation, and ICU days (103). Similar results were seen in an RCT using a fluid resuscitation protocol incorporating pulse-pressure variation in patients undergoing high-risk general surgery (104). In an attempt to find less invasive techniques to obtain the same information, investigators showed that respiratory variations in pulse oximetry waveform amplitude predicted fluid responsiveness in anesthetized patients undergoing cardiac surgery (105).

Pharmacologic investigations in cardiac surgical patients showed that perioperative hydrocortisone, when added to metoprolol, reduced the incidence of atrial fibrillation without increasing infectious complications and that aprotinin for intraoperative hemorrhage control, when compared with aminocaproic acid or tranexamic acid, was associated with increased mortality (106–108). Subsequently, the sale of aprotinin was

suspended pending review of results from an RCT of antifibrinolytic medications in cardiac surgery.

Trauma, Burns, and Poisoning

A secondary analysis of an RCT found that the survival and neurologic outcomes of out-of-hospital cardiac arrest with experienced physician-directed resuscitation were not different between trauma and medical patients, suggesting that ongoing resuscitation after out-of-hospital cardiac arrest should be considered in some trauma patients (109). Two single-center cohort studies suggested a survival benefit when traumatically injured patients received β -blockers in hospital, although the positive finding in one study disappeared in an analysis designed to limit immortal time bias (110, 111). Another cohort study raised interesting questions by finding that patients with severe brain injury from blunt head trauma have lower mortality if admitted with a low to moderate (vs. zero) blood alcohol concentration and a higher mortality if admitted with a high blood alcohol concentration (112). Although the use of anabolic steroids in the chronically critically ill is controversial, one single-center RCT in burn patients found that oxandrolone shortened length of hospital stay and maintained lean body mass without adversely affecting the endocrine axis. This therapy was associated with an increase in transaminases, suggesting the therapy may affect the liver (113). Finally, secondary analyses of an RCT of hyperbaric oxygen therapy for carbon monoxide poisoning suggested that treatment benefit is affected by age, duration of carbon monoxide exposure, and apolipoprotein E genotype (114, 115).

Neurointensive Care

The optimal manipulation of cerebral hemodynamics in treatment algorithms for brain injury remains unclear. One small cohort study suggested that transcranial-Doppler-directed therapy compared with invasive cerebral monitoring in severely brain-injured patients was practical and enabled earlier identification of brain hypoperfusion and achievement of therapeutic objectives (116). In contrast to previous work, little correlation was found between cerebral perfusion pressure and global cerebral blood flow measured by xenon-computed tomography in patients with severe head injury, suggesting preservation of pressure autoregulation (117). Positron emission tomography detected deleterious effects of hyperventilation on cerebral blood flow that were unrecognized using jugular venous saturation (118). The optimal hemoglobin target for the injured brain remains controversial. One single-center cohort study of patients with subarachnoid hemorrhage found improved functional outcomes with higher hemoglobin values (119). A number of publications showed that decompressive craniectomy substantially improves survival and neurologic outcomes in young patients with malignant middle cerebral artery syndrome (120, 121). One study of 21 patients meeting clinical criteria for brain death found a compatible electroencephalogram in all cases but intracranial arterial opacification on cerebral computed tomographic angiography in 10 patients (122).

Sedation and Analgesia

Two studies examined current sedation and analgesia practices in the United States and France (123, 124) and found the following: infrequent global nursing assessments (rare at night), oversedation despite minimally arousable or motionless patients (124), and underuse of sedation assessments and inadequate management of analgesia during painful procedures (123). Novel pharmacologic strategies included remifenataniol for poor tolerance of noninvasive ventilation for acute respiratory failure (125) and dexmedetomidine for mechanically ventilated patients (126). In

the latter study, patients were randomly allocated to dexmedetomidine or lorazepam infusions with dosing titrated according to a sedation scale; use of dexmedetomidine resulted in fewer days in coma but no difference in delirium or duration of mechanical ventilation.

Endocrinology

Steroids and the adrenal axis. Several studies advanced our understanding of adrenal insufficiency. In patients with sepsis, adrenal insufficiency is likely when baseline cortisol levels are less than 10 mg/dl or delta cortisol (after cosyntropin stimulation) is less than 9 mg/dl, yet unlikely when cosyntropin-stimulated cortisol level is 44 mg/dl or greater, or delta cortisol is 16.8 mg/dl or greater (127). Other researchers showed that cortisol levels predict severity and outcome in community-acquired pneumonia and are better than routinely measured laboratory parameters such as C-reactive protein or leukocyte count (128).

Glucose control. The risks and benefits of tightly regulated glucose in different ICU populations was an area of intense investigation yielding conflicting results. A nurse-driven computerized insulin protocol in combination with bedside glucose measurement resulted in acceptably low glucose levels with very few episodes of hypoglycemia (129). In a single ICU, failure to strictly control blood glucose despite intensive insulin therapy was common and independently associated with ICU mortality (130). In a subset of medical patients enrolled in an RCT of intensive insulin therapy and remaining in the ICU for at least 7 days, those assigned to intensive insulin therapy had a reduced incidence of critical illness polyneuropathy and myopathy, and required prolonged mechanical ventilation less frequently (131). Rigorous intraoperative glycemic control during cardiac surgery when added to postoperative glycemic control did not reduce perioperative death or morbidity but was associated with an increased incidence of death and stroke in the intensive treatment group during follow-up (132).

Renal Physiology and Dysfunction

Although recent publications have advanced understanding of the epidemiology of acute renal failure in critically ill adults, fewer data are available for children. One single-center cohort study found the incidence of acute renal failure in the pediatric ICU to be 4.5%, with independent risk factors being thrombocytopenia, older age, hypoxemia, hypotension, and coagulopathy; mortality was 29.6% (133). One study added high preoperative arterial pulse pressure to the list of risk factors for acute renal failure in adults after cardiac surgery (134). Another cohort study showed that the presence of malignancy had no independent effect on outcomes of ICU renal replacement therapy, when adjusted for organ dysfunction and timing of renal function deterioration (135).

Effective prevention and treatment strategies for critically ill patients with acute renal failure remain elusive. An RCT found no effect of *N*-acetylcysteine on the incidence of acute renal failure when administered to patients with clinically important hypotension (136). A small RCT showed similar small-molecule clearance between continuous venovenous hemofiltration and extended daily dialysis with filtration, although acidosis was better controlled by the continuous technique (137). A multinational cohort study showed that use of continuous renal replacement therapy compared with an intermittent technique was not a predictor of hospital survival or dialysis-free hospital survival but did independently predict renal recovery among survivors (138). Anticoagulation remains a requirement of continuous renal replacement therapy, and a small randomized crossover trial found intravenous enoxaparin titrated to anti-factor Xa activity to be a safe alternative to heparin (139).

INTERESTING HYPOTHESES

Many critical illness syndromes remain incompletely understood, and investigators continue to advance novel hypotheses for etiology, treatment, and prognosis. In patients who were active smokers and admitted to a medical ICU, a retrospective cohort study showed that nicotine replacement therapy was an independent risk factor for hospital mortality (140). Other studies have examined the predictive ability of novel biomarkers. The presence of nucleated red blood cells in blood strongly predicted death in a prospective cohort study (141). The apolipoprotein E4 allele, a genetic marker of Alzheimer's disease, was associated with duration of delirium in mechanically ventilated patients (142). Elevated serum S-100B protein, a calcium-binding protein predominantly in the cytosol of astroglial and Schwann cells, independently predicted 1-month survival in severe head injury, with changes during early ICU admission correlating with clinical status and surgical intervention (143).

PRACTICAL CLINICAL POINTERS

One RCT (144) and two before–after studies (145, 146) found increased diagnostic yield with a strategy of “on demand” versus routine daily chest radiographs, which also decreased the number of radiographs performed without evidence of harm. Radiation exposure, primarily from computed tomography scans, was found to confer a small excess risk of cancer and cancer-related mortality in severely injured trauma patients (147).

One study reported an incidence of central venous catheter erosion of 0.28 per 1,000 catheter-days in patients receiving total parenteral nutrition, with a higher risk for left-sided catheters and elderly patients (148). By analyzing chest computed tomography scans, investigators found that the most successful and safest technique for needle decompression of suspected tension pneumothorax was use of a needle at least 7 cm long, inserted perpendicular to the horizontal plane in the mid-hemithoracic level at the level of the sternal angle (149).

Medical educators have recently started to exploit the potential of multimedia techniques to enhance critical care learning. In 2007, procedural instruction videos were published for general central venous catheterization (150), catheterization of the subclavian vein (151), chest-tube insertion (152), bag-mask ventilation (153), and oral endotracheal intubation (154). Of the clinical images published in 2007 of interest to intensivists, two of particular interest included paradoxical embolism through a patent foramen ovale (155) and occlusion and reopening of the middle cerebral artery after thrombolysis (156).

Finally, investigators conducted a large RCT of bowel management routines and found that lactulose and polyethylene glycol are more effective in promoting defecation than placebo (157).

ICU ORGANIZATION

ICU Organization and Regional Differences in Care Delivery

An observational study conducted in European ICUs found an association of both the religious affiliation of the patient and physician on the type of end-of-life decision, the times to therapy limitation and death, and discussion of decisions with patients' families (158). A Canadian study found that, among patients 50 years or older, women appear less likely than men to be admitted to ICU and less likely to receive selected life-supporting therapies (159). A survey observed that Medicare beneficiaries generally prefer treatment focused on palliation rather than life extension, yet these preferences are unlikely to explain regional variations in end-of-life spending (160). A complementary study demonstrated wide unexplained variability in length of stay of

nonsurvivors after cardiac arrest, suggesting variation in the timing of end-of-life decisions (161).

Physician Training and Work Hours

The Accreditation Council for Graduate Medical Education implemented duty hour regulations for physicians-in-training throughout the United States in 2003. One large retrospective cohort study found no difference in hospital mortality rates among Medicare beneficiaries in U.S. nonfederal hospitals, and a reduction in mortality due to four common medical conditions in Veterans Administration hospitals after this change (162, 163). A single-center study highlighted a higher complication rate for adult trauma patients admitted in the 2 years before introduction of a maximum 80-hour work week (164). A survey of internal medicine residents documented that most feel unprepared and unsupervised as cardiac arrest team leaders in teaching hospitals (165).

Communication

Policies of increasingly open ICU visiting hours were perceived favorably by families, but less so by ICU nurses due to concerns about care interruption (166–168). Data from pediatric ICUs indicated limited interruption of rounds due to parental presence (169).

ICU Health Care Professional Burnout

Burnout is common among ICU nurses and physicians and is associated with increased workload and impaired relationships among colleagues (170, 171). ICU nurses have a higher rate of post-traumatic stress disorders than other nurses and this was associated with less flexible scheduling, poor working relationships, and increased end-of-life care (172, 173).

Models of Initiation, Delivery, and Transfer of Critical Care

Using the project IMPACT database, it was found that critically ill emergency department patients with more than a 6-hour delay in ICU transfer experienced increased mortality (174). Twenty-four-hour per day on-site intensivist coverage was associated with improved processes of care, staff satisfaction, and reduced length of ICU stay (175), whereas increased nursing staffing reduced ICU infections and hospital mortality (176–180). Observational studies using simulation found that increasing transfers of acutely ill patients away from hospitals might decrease their standardized mortality ratio (181) and that regionalization of some aspects of critical care may improve survival for patients undergoing mechanical ventilation (182).

Outreach, Rapid Response, and Medical Emergency Teams

Many hospitals have begun to deploy outreach teams to aid in the care of acutely ill patients outside the ICU. Despite a previous large cluster RCT failing to document benefit, before–after trials evaluating outreach services continue to show fewer cardiac arrests, faster time to treatment, and fewer unplanned ICU admissions, yet limited evidence to support changes in mortality (183–188). Early warning triggers still have imperfect sensitivity for detecting at-risk patients (189); multifaceted strategies aid in optimal deployment of outreach services (190).

KNOWLEDGE TRANSLATION

Critical care, like all fields in medicine, must address the fact that publishing studies of effective interventions does not ensure that patients receive their benefits. Recent studies have identified the barriers likely to be encountered in implementing early goal-directed therapy for sepsis (recognition of sepsis in emergency

room, monitoring of central venous pressure, handoff to ICU) (191), using lung-protective ventilation for ALI (192), creating intensivists-staffed ICUs in the United States (loss of patient control, loss of income, and cost to hospital) (193), and improving communication among providers in the ICU (nurses and physicians have different perceptions of the quality of communication) (194). Qualitative research has demonstrated that different providers have different perspectives on the barriers and solutions to knowledge translation using lung-protective ventilation for ALI (195).

Guidelines

Important critical care guidelines were published in 2007 summarizing the management of patients with traumatic brain injury (196), appropriateness criteria for transthoracic and transesophageal echocardiography (197), ways of supporting the family in the patient-centered ICU (198), and clinical management of patients with an influenza-like illness during an influenza pandemic (114). Other guidelines were published to inform the conduct of research on medical emergency teams (199) and for implementation of community consultation and public disclosure regarding research protocols (200).

QUALITY

A new system for ICU prognostication and risk adjustment was developed in the United Kingdom (201). Other groups developed tools for predicting acute renal failure after cardiac surgery (202) or mortality after renal failure in general ICUs (203). Meanwhile, investigators demonstrated that classification of “high performing” versus “low performing” ICUs often depended on which risk adjustment score was used, suggesting that ICU ranking by a single instrument is problematic (204). To address this limitation, there has been renewed interest in developing more practical methods for measuring evidence-based process-of-care indicators (e.g., semirecumbent positioning) to assess the quality of ICU care (205).

ETHICS

Confirming other work, a single-center before–after evaluation suggested that proactive palliative care consultation in certain high-risk groups was associated with a shorter ICU length of stay but no statistically significant differences in mortality or discharge disposition (206). Data collected from European ICUs also raised concerns that there is not a clear distinction between treatments administered to relieve pain and suffering versus those intended to shorten the dying process (207).

A survey of physicians suggested that incapacitated patients without surrogates accounted for approximately 1 in 20 deaths in ICUs, and most life-support decisions for these patients were made by physicians without institutional or judicial review (208). A survey of practice since the passing of the Texas Advance Directives Act, which provides legal immunity for physicians who discontinue life-sustaining treatment judged to be medically inappropriate, showed that only a minority have used these new policies and procedures to review specific patient cases (209). Researchers used semistructured interviews of physician directors, nurse managers, and respiratory therapists from Canadian ICUs to propose a new working definition of medically futile care that included the use of considerable resources without a reasonable hope that the patient would recover to be interactive with his or her environment (210). In the United Kingdom, an observational study of 92 ICUs suggested that clinicians may be inappropriately pessimistic about the outcomes of critically ill

patients with chronic obstructive pulmonary disease and, as a result, may limit beneficial life-sustaining treatments (211).

Research Consent

A qualitative study of researchers and patients with cancer highlighted some of the challenges of researching end-of-life care, including the difficulty of defining the end of life, gatekeeping by ethics committees and clinical staff, the need to consider high attrition rates associated with deterioration or death, and managing the emotions of participants and research staff. This study found that many people nearing the end of life do want to be offered the chance to participate in research, provided it is conducted with sensitivity (212).

In one study, 80% of ICU survivors recognized, 10 to 12 days after informed consent had been obtained, that they had participated in a clinical trial, but only one-third could recall the clinical trial purpose and its related risks. More patients with complete recall had read the information leaflet or asked at least one question before signing the informed consent (213). Another study suggested that the majority of community meeting attendees understood basic concepts and regulations of emergency research without prior consent. However, despite 82% concurrence with the study in their community, approximately 30% of persons would not willingly choose to participate in emergency research or provide consent for their family members despite knowledge about the process (214).

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