42nd Critical Care Congress Review

Supported by education grants from Hospira, Inc. and Nestlé HealthCare Nutrition.

CE/CME Enduring Material
Release Date: June 2013
Expiration Date: June 2014

Learning Objectives

At the conclusion of this activity participants should be able to:

- Discuss approaches to screen for delirium and consider both pharmacologic and nonpharmacologic approaches to prevention and management
- Minimize the development of malnutrition through goal-directed therapy combining the use of enteral and parenteral nutrition
- Recognize new therapies for sepsis in the intensive care unit and the limitations of current research for better translation of evidence to the bedside

Type of Activity

This activity was designed as an evidenced based forum to review expert opinions of various topics in critical care. This activity will focus on increasing knowledge and its application to practice.

Competencies

SCCM supports recommendations that will promote lifelong learning through continuing education. SCCM promotes activities that encourage the highest quality in education that will enhance knowledge, competence or performance in critical care practice. This activity will meet the following:

- Patient- and Family-Centered Care
- Practice Applications
- Quality Improvement
- Multiprofessionalism

Target Audience

This continuing medical education offering is intended to meet the needs of all physicians, nurses, pharmacists, respiratory therapists and other providers who care for critically ill patients.

Physicians

Accreditation Statement

The Society of Critical Care Medicine (SCCM) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Designation Statement

SCCM designates this home study educational activity for a maximum of 1 AMA PRA Category 1 credits™. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Nurses

SCCM is approved by the California Board of Registered Nursing, Provider No. 8181 and approves this panel for 1 contact hour.

Pharmacists

The Society is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmaceutical education. This monograph will provide 1 continuing education hour. (0236-0000-13-469-H01-P) SCCM reports to a continuing pharmacy education (CPE) tracking service, CPE Monitor that will authenticate and store data for completed CPE units received by pharmacists and pharmacy technicians. The tracking system will make CPE data for each participant available to the state boards of pharmacy where the participant is licensed or registered. After CPE units are processed by ACPE and NABP, pharmacists and pharmacy technicians will be able to login to a comprehensive electronic profile to access information about their completed CPE.

Obtaining Credit

To claim credit, a learner must purchase the free course via the SCCM store at www.sccm.org/CongressReview13. There is no cost for this transaction.

Upon completion of this free purchase and the complete review of the material, please login to www.mysccm.org with your SCCM Customer ID and password. In the My Learning section of MySCCM.org, links will appear for this activity's posttest and evaluation under Congress Review. After earning a passing score of 70% or higher on the posttest, you will be able to claim credit for this activity.

For more information on the Congress Review, please contact SCCM at **support@sccm.org** or call **+1 847 827-6888.**

For additional information on these topics and other areas, please visit **www.learnicu.org**

Disclosures

The content of this activity has been peer reviewed and has been approved for compliance. The activity planners, SCCM staff member Adair Andrews and other employees of SCCM, have no financial relationships to disclose. The faculty and contributors have indicated the following financial relationships, which have been resolved through an established conflict of interest resolution process and have stated that these reported relationships will not have any impact on their ability to provide unbiased content.

Juliana Barr, MD, FCCM
Veterans Affairs Palo Alto Health Care Systems
Palo Alto, California, USA
No financial relationships

Richard J. Beale, MD, MBBS, FRCA, FFICM
Saint Thomas' Hospital
London, United Kingdom
Studies/Consulting – Eli Lilly

Judy E. Davidson, RN, CNS, DNP, FCCM
Scripps Clinical Research Center
La Jolla, California, USA
Speakers Bureau – France Foundation

R. Phillip Dellinger, MD, MCCM
Cooper University Hospital
Camden, New Jersey, USA
No financial relationships

Niall D. Ferguson, MD
Toronto Western Hospital
University
Toronto, Ontario, Canada
In-kind Support – CareFusion

Ramona O. Hopkins, PhD
Intermountain Medical Center
Murray, Utah, USA
No financial relationships

Theodore J. Iwashyna, MD, PhD
University of Michigan Health System
Ann Arbor, Michigan, USA
No financial relationships

Aaron M. Joffe, DO
University of Washington
Harborview Medical Center
Seattle, Washington, USA
No financial relationships

Amal Jubran, MD
Edward Hines Jr. Veterans Affairs Hospital
Washington, DC, USA
No financial relationships

Mitchell M. Levy, MD, FCCM
Brown University
School of Medicine
Providence, Rhode Island, USA
No financial relationships

Ainsley Malone, RD
Mount Carmel West
Columbus, Ohio, USA
Speakers Bureau – Abbott Nutrition

Robert G. Martindale, MD, PhD
Oregon Health & Science University
Portland, Oregon, USA
Speakers Bureau – Lifecell, Nestle

Andrew Rhodes, MD
St. George's Hospital
London, United Kingdom
Director; Provider of Healthcare – Lilly, LiDCO

Sean R. Townsend, MD
California Pacific Medical Center
San Francisco, California, USA
No financial relationships

Paul Wischmeyer, MD
University of Colorado at Denver School of Medicine
Aurora, Colorado, USA
Consultant, Research Grant Recipient
Occasional Speaker – Baxter
Grant, Consultant, Occasional Speaker – Abbott
Research Grant, Consultant – Fresenius Inc.

Late Breaker: The Latest in Critical Care Research

Recent controlled trials have uncovered important findings for intensive care units (ICUs) as well as long-term care facilities. These studies take a look at strategies for weaning patients from prolonged mechanical ventilation to the use of high-frequency oscillation in acute respiratory distress syndrome.

Weaning from Prolonged Mechanical Ventilation

Presented by Amal Jubran, MD, a Physician at the Edward Hines Jr. Veterans Affairs Hospital in Hines, Illinois, USA.

Patients who require prolonged mechanical ventilation (>21 days) account for 13% of ventilated patients and consume 37% of ICU costs. Such patients are transferred to long-term acute care hospitals, where costs have risen dramatically (Kahn JM, et al. *JAMA*. 2010;303:2253-2259). "Prospective research into strategies that can expedite weaning at long-term acute care hospitals are virtually nonexistent," said Amal Jubran, MD, who reported on her recent randomized study of weaning technique outcomes.

"We know that ventilator duration in ICU patients is influenced by weaning methods," Jubran said. The two most common are pressure support and spontaneous breathing trials, but the relative efficacy of these methods has previously undergone no scrutiny in patients managed at long-term acute care hospitals.

Jubran's study involved patients transferred to a long-term acute care hospital for weaning from prolonged ventilation (Jubran A, et al. *JAMA*. 2013;309:671-677). "We compared the length of time required for weaning with pressure support versus unassisted breathing through an O_2 delivery device connected to a tracheostomy tube (a tracheostomy collar)," she said. "In the pressure-support arm, level of pressure was decreased by 2 cm H2O three times a day. When a patient was able to tolerate a pressure support of < 6 cm H2O for at least 12 hours, the patient was disconnected and allowed to breathe without assistance through the tracheostomy. In the trach-collar arm, patients were disconnected from the ventilator and allowed to breathe through the tracheostomy for a maximum of 12 hours during the first two days. On the third day, patients were allowed to breathe unassisted through the tracheostomy up to a maximum of 24 hours each day. We also determined the six-month and 12-month survival data for these patients." Weaning duration – the study's primary outcome measure – was defined from the first day of randomization to the day the patient was successfully weaned (i.e., breathed without ventilator assistance for at least five days).

Of the 500 patients enrolled, 184 were not randomized, primarily because they passed the initial screening test. "This finding suggests that one third of patients transferred to long-term acute care hospitals could have been weaned in the ICU," Jubran said. The 312 randomized patients (average age: 69 years) received either tracheostomy collar weaning or pressure support weaning. Causes of respiratory failure were evenly split between cardiopulmonary disorders and postsurgical complications.

"In comparing our data with ICU data, we found that the demographics did not differ with the exception of days on mechanical ventilation, which was about eightfold higher among our patients than ICU patients," said Jubran. "All the physiological variables measured on enrollment were comparable for ICU and long-term acute care hospital patients, indicating that our patients are no different from ventilated patients who are managed in an ICU."

The study showed that weaning duration was shorter with the tracheostomy collar (15 days) than with pressure support (19 days). Among successfully weaned patients, the difference was even greater: 11 days for the tracheostomy collar group versus 16 days for the pressure support group. "After adjusting for the baseline covariates that can influence weaning duration using a Cox proportional hazard model, the rate of successful weaning was 1.43 times higher with a trach collar than with pressure support," reported Jubran.

Other results revealed that mortality during the study and 12 months after discharge were equivalent in both groups. "It's important to point out that our study was not powered to detect a difference in mortality rates between the two arms," said Jubran. "We did look at one-year survival for all 500 (randomized and nonrandomized) patients, and we found that 54% and 45% were alive at six months and 12 months after discharge, respectively. To put this number in perspective, the one-year survival rate of elderly patients ventilated in the ICU was on average 40%. Patients in our study who received mechanical ventilation for 67 days had a one-year mortality rate comparable to ICU patients who received ventilation for nine days."

A comparison of survival curves for weaning successes versus failures showed even more impressive differences. At 12 months, survival was 4.4-fold higher in weaning-success patients (72%) than in weaning-failure patients (16%).

Jubran proposed reasons why her randomized controlled trial demonstrated a positive outcome when the majority of other critical care trials have not. "First, the physiological rationale for undertaking our study was based on several physiological experiments that we previously conducted," said Jubran. These experiments showed that the workload on respiratory muscles was higher in weaning-failure patients versus weaning-success patients, and this was due to progressive increases in resistance, elastance and intrinsic positive end-expiratory pressure (PEEP) (Jubran A, et al. *Am J Respir Crit Care Med*. 1997;155:905). Other studies showed that pressure support is not as good as assist-control ventilation in resting the muscles and can, for example, cause patient-ventilatory dyssynchrony (Jubran A, et al. *Am J Respir Crit Care Med*. 1995;152:129-136).

Another set of experiments demonstrated that the contraction of expiratory muscles before the end of mechanical inflation interferes with the ability of the next inspiratory effort to trigger the ventilator, therefore leading to non-triggering (Parthasarathy S, et al. *Am J Respir Crit Care Med*. 1998;158:1471-1478). "We have also shown that pressure support fosters instability of the respiratory control system during sleep by producing central apneas that do not occur during assist control," said Jubran.

"The slower pace of weaning with pressure support we found in our trial may be related to its effect on clinical decision making," Jubran stated. "Observing a patient breathing through a trach collar provides a clear view of the patient's respiratory capabilities, whereas with pressure support, it's difficult to distinguish between how much the patient is doing and how much the ventilator is doing."

The fact that the present study was confined to a single center may be another reason for the positive outcome. "It's important in research to minimize systematic errors by controlling for confounding variables, and we were able to do so by restricting the trial to a single site. That gave us greater internal validity than can be achieved with multiple site trials."

"We concluded that use of a trach collar significantly improves the outcome of patients who require prolonged ventilation at a long-term care facility," said Jubran.

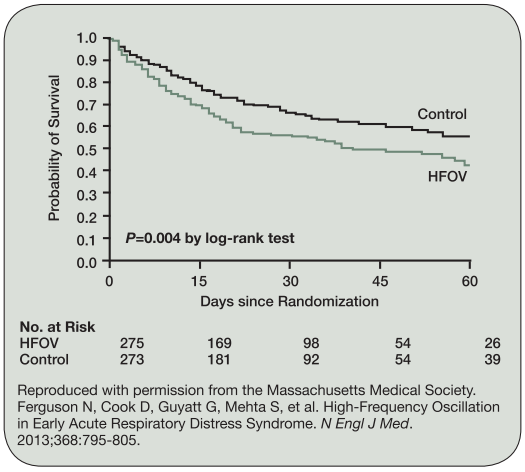
Oscillation for Acute Respiratory Distress Syndrome Treated Early: The OSCILLATE Trial

Presented by Niall D. Ferguson, MD, MSc, FRCPC, Director of Critical Care Medicine at University Health Network and Mount Sinai Hospital, and Associate Professor of Medicine and Physiology in the Interdepartmental Division of Critical Care Medicine at the University of Toronto, in Toronto, Ontario, Canada.

Given the high mortality associated with acute respiratory distress syndrome (ARDS), clinicians will be interested in learning about the results of the recently published OSCILLATE trial, which evaluated the effects of using high-frequency oscillation in early ARDS (Ferguson ND, et al. *N Engl J Med.* 2013;368:795-805). This international, multicenter, randomized trial – funded by the Canadian Institutes of Health Research and conducted in collaboration with the Canadian Critical Care Trials Group – produced unexpected results that have important implications in the ICU.

"Theoretically, high-frequency oscillation is ideal for lung protection," said Niall D. Ferguson, MD, MSc, FRCPC, one of the trial's co-investigators. "By delivering very small tidal volumes at a relatively constant mean airway pressure, we should theoretically be able to get into a safe window and protect the lung," he said. Several case series have shown improvement in oxygenation when adults with ARDS received high-frequency oscillation. Moreover, randomized controlled trials performed in the 1990s suggested that high-frequency oscillation reduced mortality among adults with ARDS. "These trials, however, were small and used outdated ventilation strategies," noted Ferguson.

Kaplan-Meier Curve for High-Frequency Oscillation Versus (HFOV) Conventional Ventilation (Control)



Reproduced with permission from the Massachusetts Medical Society. Ferguson N, Cook D, Guyatt G, Mehta S, et al. High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome. *N Engl J Med*. 2013;368:795-805.

Figure 1.

The limitations of these studies led the OSCILLATE investigators to their research question: For critically ill adults with ARDS, does the early application of high-frequency oscillation (HFO) reduce hospital mortality in comparison to a high PEEP, low tidal volume ventilation strategy that incorporates HFO exclusively as a "rescue" therapy? "Essentially, we were asking whether we could reduce ventilator-induced lung injury through use of high-frequency oscillation ventilation," said Ferguson.

Following a pilot phase, the full randomized controlled trial was conducted from 2009 through 2012, with 1,200 patients meeting criteria for ARDS. "Our HFO strategy was built on our pilot physiological study as well as recommendations from an expert panel published the previous year," Ferguson reported. "We were trying to get the lung open and oscillate on the deflation limb of the volume pressure curve. Initial settings were a mean airway pressure of 30, a ΔP of 90, and pressure amplitude of 90. Then we used the highest frequency we could to deliver an acceptable pH, enabling us to ensure that the lowest tidal volume would be delivered with HFO."

The trial's oxygenation protocols utilized tables with variable levels of PEEP FIO_2 and mean airway pressure FIO_2 for the control and HFO groups. When the mean airway pressure reached 20 to 24 cm H_2O and the FIO_2 was 40%, HFO patients transitioned to the conventional protocol.

Several safety initiatives were in place throughout the trial, and interim analyses included safety reviews at 300, 500 and 700 patients being randomized. "These reviews looked at physiological data and use of vasopressors, barotrauma and neuromuscular blocker use," said Ferguson. "If the reviewers detected anything of concern, they could request an unscheduled mortality evaluation."

At the recommendation of the data monitoring committee, the trial was stopped after 548 patients had undergone randomization. Of these, 270 received HFO and 273 received the control ventilation. The groups were well-matched at baseline. The HFO group received this therapy for a median three days, and 81% moved to conventional ventilation after a median three days. In the control group, 12% of patients were converted to HFO after a median of two days, and they received HFO for a median of seven days.

"Our main results did not match our hypothesis," reported Ferguson. "We found an excess number of deaths in the HFO group – 47% versus 35% for all-cause, in-hospital mortality. This result was consistent when we looked at death in the ICU and death at 28 days." As shown in Figure 1, the difference in mortality emerged early in the trial.

The results also showed a numerically greater, but not statistically significant, difference in the increase in new barotrauma (18% for HFO vs. 13% for control). Although fewer patients in the HFO group developed refractory hypoxemia, the total number of deaths among these patients was similar in both groups. "Of less relevance, given the mortality changes, was the finding that there were no differences in duration of mechanical ventilation or ICU stay among survivors," Ferguson added.

Subgroup analyses, which included a group of patients with baseline hypoxemia, also revealed that mortality was higher in the HFO versus the control group. More patients in the HFO group received vasoactive and opiate drugs compared with the control group.

"We concluded that HFO as used in our trial does not improve survival and is likely harmful compared with a high PEEP, low tidal volume conventional strategy allowing only HFO as a rescue therapy," stated Ferguson.

"I think our results have important implications for care," Ferguson continued. "They raise serious concerns about using HFO early as a primary lung protective strategy, and increase the uncertainly about the benefits of HFO as a rescue therapy."

Continuing Education Self-Assessment

Late Breaker

5. How did tracheostomy collar weaning compare with pressure support weaning in patients on prolonged mechanical ventilation?
   a. Mortality during the study and 12 months after discharge was higher in the pressure support weaning group.
   b. The rate of successful weaning was 1.4 time higher with the tracheostomy collar.
   c. The duration of weaning was statistically similar with both weaning methods.
   d. Weaning duration was 8 days with tracheostomy collar and 15 days with pressure support weaning.

6. Compared with a positive-end-expiratory-pressure, low-tidal-volume conventional strategy, high-frequency oscillation was associated with:
   a. An excess number of deaths.
   b. A decrease in new barotrauma.
   c. An increase in refractory hypoxemia.
   d. Fewer ICU days among survivors.