Fluid Resuscitation in Acute Respiratory Distress Syndrome and Sepsis

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Acute respiratory distress syndrome (ARDS) and sepsis: clinical states involving marked abnormalities of microcirculation (capillary leak), with abnormal perfusion of tissue and abnormal cellular function; most common comorbidity associated with sepsis; outcomes improved if initial hypoperfusion prevented; confusion often exists about quantity and type of fluids to administer

Sepsis: pneumonia most common cause in lung, with ARDS developing afterward (ARDS can be considered pneumonia of entire lung); other organs also sustain damage; seriously ill patients have better outcomes when transferred to large medical center; study of data from Medicare database shows that centers and physicians with more experience treating sepsis or ARDS have lower mortality rates

Goal-directed therapy: standard resuscitation, without protocols, started ≥12 hr after admission does little to improve outcome; early (≤6 hr after admission) goal-directed approach using treatment protocol improves outcomes; protocolized care alone shown to decrease mortality by 10%

Issues for treatment: infection — give correct antibiotics early; eradicate source of infection (if possible); resuscitate with fluids to reverse hypotension; consider whether to base treatment on pulmonary artery occlusion pressure (PAOP), central venous pressure (CVP), or mixed venous oxygen saturation (SvO2); management — delay of appropriate antibiotics increases mortality by ≈10% per hour of delay; however, administration of inappropriate antibiotics increase mortality by ≤50% (blood cultures should be drawn first so that spectrum can be narrowed as soon as results available); mechanical ventilation — minimizing lung stretch has significant effect on mortality; use of either 6 mL/kg ideal body weight or 28 cm H2O plateau airway pressure lowers risk for mortality, but not guaranteed to prevent lung injury; normal-tidal-volume ventilation should be maintained in operating room (high tidal volume of 10 mL/kg originally used to prevent atelectasis); prone positioning improves outcome for patients with severe ARDS

Protocolized care: in Rivers study, significantly higher fluid resuscitation seen within first 6 hr in group that received early goal-directed therapy, compared with control group, despite administration of equivalent volumes over 72-hr period; data on patients with acute pancreatitis show early resuscitation (≥23% of all fluids administered in first 24 hr of 72-hr window) results in less systemic inflammation response syndrome (SIRS), less organ failure, decreased intensive care unit (ICU) admissions, and reduced hospital length of stay; limitations of protocols — surviving Sepsis Campaign guidelines promote use of activated protein C (ineffective), and tight glucose control without accurate continuous measurement of glucose (led to increased incidence of hypoglycemia [which may be more detrimental than hyperglycemia]); study from Spain showed improved outcomes with protocolized practices, but clinicians reverted to original standards after 1 yr (physician practices difficult to change); use careful selection when establishing protocols and add or eliminate elements based on outcome studies; benefits of good protocolized care dependent on duration of patient stay

Intravenous (IV) fluids: normal saline hypertonic and hyperchloremic (can cause metabolic acidosis); colloids include albumin or hydroxyethyl starch (HES) and gelatin

Crystalloids: include normal saline, Ringer’s lactate, and Plasma-Lyte; normal saline — chloride concentration equals sodium concentration (made by dissolving salt in water); hyperviscous; causes significantly lower renal blood flow and increased mortality, compared with balanced salt solution; saline should not be used unless patient in state of hypotonic hypochloremic metabolic alkalosis (rare); study showed that switching from normal saline to balanced salt solution (no other changes) decreased mortality

Colloids vs crystalloids: according to traditional medical education, crystalloids distribute into interstitial space, while colloids remain restricted to plasma space (provide more effective volume expansion); glycocalyx — maintains difference in permeability; greatly affected by drugs and disease (eg, sepsis); administration of anesthetic drugs profoundly alters volume of distribution of IV fluids; colloids — half-life theoretically longer; however, HES and gelatin can trigger allergies, coagulation problems, and renal failure; HES not metabolized (crystals remain in kidneys, skin, and brain); with profound alteration of glycocalyx, both colloids and crystalloids able to pass into interstitial space, thereby promoting continued fluid movement into interstitium (colloid osmotic pressure increased); therefore, colloids should be avoided in ARDS and sepsis (presence in interstitium promotes fluid retention); recommendations — albumin safe to use (benefit unknown, but induces no harm); HES causes harm and increases mortality, so Ringer’s lactate preferred; European Intensive Care Society recommends avoidance of HES for management of patients with sepsis; most data

Educational Objectives

The goal of this program is to improve hemodynamic optimization of the perioperative patient. After hearing and assimilating this program, the clinician will be better able to:

1. Explain how protocolized care improves outcomes for patients with acute respiratory distress syndrome (ARDS) and sepsis.
2. Evaluate the benefits of crystalloid vs colloid solutions in resuscitation of patients with ARDS and sepsis.
4. Define “triple low” and recognize its effects on patient outcomes.
5. Reduce the incidence of postoperative delirium through monitoring of bispectral index (BIS) scores.

Faculty Disclosure

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Resuscitation goals: ARDS Network studied liberal vs restrictive management; compared with liberal group, restrictive group showed improved oxygenation, and ≤3.5 fewer days on mechanical ventilation and in ICU, with no difference in mortality; however, when long-term outcomes evaluated, odds ratio for impaired mental function in members of restrictive group found to be 4 times that of liberal group; conclusion — no rationale exists for withholding early aggressive resuscitation of ARDS patients

Resuscitation techniques: hypotension reduces blood flow to organs, disrupts autoregulation, induces strong sympathetic tone (causing proinflammatory and hypercoagulable state and altered immune response), and causes adrenocorticotropic hormone (ACTH) response; in context of initial resuscitation of hypotension, cardiac output (CO) only important in maintaining arterial pressure; goal blood pressure (BP) — 65 mm Hg sufficient for normal patients (no improvement in organ perfusion seen with norepinephrine or other drugs); norepinephrine preferred over dopamine (unless patient bradycardic); vasopressin recommended for support only; steroids may benefit extremely ill patients who do not respond to norepinephrine; volume of fluid — volume challenge may damage circulation (speaker recommends determining whether patient volume-responsive and resuscitating accordingly); type of fluid — use balanced salt solution; avoid normal saline, HES, and gelatin; albumin (25 g) acceptable after 3 to 4 L crystalloid; targets — CVP 8 mm Hg or PAOP 12 mm Hg proposed by group in Paris (without physiologic basis); no relationship found between blood volume and CVP (wedge pressure does not predict volume responsiveness); change in CVP or wedge pressure not related to change in stroke volume; administration of fluid results in pulmonary edema and death in presence of diastolic dysfunction (identification of location on Starling curve not possible)

Functional hemodynamic monitoring: positive-pressure breathing causes fluctuations in end-diastolic volume; variation in stroke volume or pulse pressure indicates volume responsiveness; stroke volume and pulse pressure have linear relationship; volume responsiveness directly proportional to amount of variation in pulse pressure; stroke volume and variation in pulse pressure both extremely accurate; low CVP indicates low probability of volume unresponsiveness, and increasing variation in pulse pressure indicates increased responsiveness (all patients volume responsive when pulse pressure >20%); visible variation in pulse pressure on monitor indicates pressure >15%; arterial tone — hypotension always pathologic, but normotension does not indicate health; increasing stoke volume (on beat-to-beat basis) increases pressure; decreased mean arterial pressure (MAP) for given stroke volume (SV) indicates decreased vasomotor tone; conversely, increased MAP for same SV indicates increased vasomotor tone; when assessing dynamic elastance (pulse pressure-to-SV variation), systemic vascular resistance, mean pulse pressure-to-SV ratio (shock index), and mean arterial pressure, only pulse pressure-to-SV variation (at values >0.9) predict increase in BP in response to increased CO

Basic plan: correct hypotension with fluids and norepinephrine; optimize oxygen delivery with further fluids and dobutamine (if no response)

Protocol for management of septic shock: first, determine whether patient stable; if not, determine whether patient volume responsive (variation in SV or pulse pressure >15% on positive-pressure breathing, or increased CO of ≥10% with passive leg-raising); assess whether patient has hypotension and decreased vasomotor tone (variation in pulse pressure divided by variation in SV); 50% of patients volume responsive; if patient hypotensive only, treat with volume and norepinephrine; vasopressor required for patients unresponsive to volume and hypotensive with decreased vasomotor tone (due to, eg, spinal anesthesia, septic shock after fluid resuscitation); if unstable and unresponsive to fluid, patient may be hypotensive, but if vasomotor tone not decreased, cause unclear; start dobutamine while performing further diagnostic studies to determine etiology (eg, pulmonary embolism, tamponade, myocardial infarction), and reassess in 15 min

Key points: Surviving Sepsis guidelines contain important concepts; obtain blood culture before administering antibiotics to narrow broad spectrum; measure lactate (clearance and acid-base status); aggressively treat hypotension with balanced salt solution; if patient not previously hypertensive, MAP 65 mm Hg sufficient (titerate up); assess organ function; ignore right atrial pressure and CVP as resuscitation targets (use functional measures); prevent further injury with pressure-limited ventilation, fluids, and norepinephrine for hypotension (with or without vasopressin), and follow protocols

Goal-Directed Anesthesia: Preventing the Triple Low

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Triple low: aggregate purported to influence long-term outcomes related to anesthesia care, and involves triad of low mean alveolar concentration (MAC), low bispectral index (BIS), and low MAP; present in 6% to 46% of noncardiac anesthetics; low BIS combined with low MAC indicates anesthetic sensitivity; relative risk increases for each minute of low MAP (<75 mm Hg); actions and events in operating room have direct effect on patient outcomes; management of triple low involves management of BP, consciousness monitors, anesthesia outcomes, and mortality with inhalational anesthetic; double low — defined in study by Monk in 2005; relative risk shown to increase for every minute systolic BP remains low (effect magnified by concurrent low BIS); American Society of Anesthesiologists class greatest predictor of poor outcome at 1 yr, but association with poor outcome observed in patients with low BP and low BIS levels; additional data show mortality increased at 1 yr in patients with low MAC (odds ratio 2.5 when combined with low BP and low MAC)

Treatment of triple-low state: observational study — found rapid administration of vasopressors reduces mortality; mortality increased by 7% when in triple-low state <5 min, but relative risk increased with increasing duration; retrospective study — triple low considered “ominous predictor”; MAC lower in nonsurvivors; 46% of patients experienced ≥1 triple-low episode during anesthesia, which improved with vasopressors

Effects of triple low: prospective observational study (2012) — triple low seen in 6% of 24,000 patients, with resulting prolongation of length of stay and quadrupling of 30-day mortality; low MAC presented isolated risk, while low MAP or low BIS did not; relative risk for mortality increased with double or triple low; patients enter high-mortality state when BIS low did not; relative risk for mortality increased with duration; triple-low state; BP, consciousness monitors, anesthesia outcomes, and mortality with inhalational anesthetic; double low — defined in study by Monk in 2005; relative risk shown to increase for every minute systolic BP remains low (effect magnified by concurrent low BIS); American Society of Anesthesiologists class greatest predictor of poor outcome at 1 yr, but association with poor outcome observed in patients with low BP and low BIS levels; additional data show mortality increased at 1 yr in patients with low MAC (odds ratio 2.5 when combined with low BP and low MAC)

Modification of BIS: BIS can be used in evidence-based fashion; postoperative delirium — low BIS scores correlate with increased risk for delirium; use of BIS monitoring may help avoid unnecessarily deep states of anesthesia and associated negative outcomes of delirium and cognitive dysfunction; increased risk for postoperative delirium observed with lower scores on preoperative Mini-Mental State Examination; if preoperative delirium present, significantly increased delirium expected for short period after surgery, continuing for ≤1 yr; increased duration of delirium portends poorer outcome; further study of association between cognitive trajectory, delirium, and BIS warranted
Hypotension: in cardiac surgery, preoperative pulse pressure known to affect outcomes (as pulse pressure widens, incidence of stroke increases); increased mortality associated with intraoperative systolic or diastolic BP outside target zone; triad of high blood loss, low BP, and high heart rate associated with increased rate of complications; additional studies show increased kidney and myocardial injury associated with low BP (MAP <55 mm Hg; kidney and cardiac outcomes worsen with increased duration of low-BP state); intraoperative management — begin goal-directed hemodynamic management (administer balanced salt solution, phenylephrine, or epinephrine or norepinephrine to improve alpha and beta profiles); BP should be kept within normal range

Mean alveolar concentration: many factors reduce MAC (eg, hypothermia, hyponatremia, hypoosmolality, acidosis, hypoxia, hypercarbia); MAC age dependent (in elderly or high-risk patients, concern for awareness occurs at lower MAC); low MAC has not been proven to cause adverse outcomes, but some studies show association; additional studies required to identify risks associated with deep hypnotic state of anesthesia (most likely, postoperative delirium or cognitive dysfunction)

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1. Improved outcomes have been seen when goal-directed therapy is started _______ after admission.
   (A) ≤6 hr  (B) ≤8 hr  (C) ≤10 hr  (D) ≤12 hr

2. Select the true statement about managing patients with acute respiratory distress syndrome (ARDS) or sepsis who are being mechanically ventilated in the operating room.
   (A) Maintenance of plateau airway pressure at 28 cm H₂O assures that no lung injury will occur
   (B) Tidal volumes should be increased for the duration of the surgery to prevent atelectasis
   (C) Use of activated protein C is associated with improved outcomes
   (D) None of the above

3. Which of the following positions is associated with improved outcomes in patients with severe ARDS?
   (A) Supine  (B) Trendelenburg  (C) Prone  (D) Left lateral decubitus

4. Which of the following statements about protocolized care for ARDS and sepsis is true?
   (A) Tight glucose control is a key component
   (B) An established protocol improves outcomes
   (C) Fluid should be restricted for the first 6 hr of the initial 72-hr window
   (D) Clinicians readily incorporate new protocols into daily practice

5. Anesthetic drugs can alter the functioning of the glycocalyx, and thereby change the volume of distribution of intravenous fluids.
   (A) True  (B) False

6. Which of the following is the vasopressor of choice for treating hypotension in cases of ARDS and sepsis?
   (A) Dopamine  (B) Dobutamine  (C) Vasopressin  (D) Norepinephrine

7. Volume responsiveness is directly proportional to:
   (A) Pulmonary artery occlusion pressure  (C) Variation in pulse pressure
   (B) Central venous pressure  (D) Mean arterial pressure

8. Triple low is defined by which of the following triads?
   (A) Low bispectral index (BIS), low mean alveolar concentration (MAC), low blood pressure (BP)
   (B) Low BIS, low BP, low heart rate (HR)
   (C) Low BIS, low BP, high blood loss
   (D) Low MAC, low BP, low HR

9. According to a prospective observational study on the effects of the triple-low state, which of the following present(s) independent risk for poor outcomes?
   1. Low MAC
   2. Low MAP
   3. Low BIS
      (A) 1, 2, and 3  (B) 2 and 3  (C) 1  (D) 3

10. Multiple brief but nonconsecutive episodes of triple-low state pose negligible risk for adverse outcomes.
    (A) True  (B) False

Answers to Audio-Digest Anesthesiology Volume 56, Issue 03: 1-A, 2-C, 3-D, 4-A, 5-B, 6-B, 7-B, 8-C, 9-B, 10-D