Critical Care April 2005 Vol 9 No 2 Rady

Review

Bench-to-bedside review: Resuscitation in the emergency department

Mohamed Y Rady

Associate Professor of Critical Care Medicine, Mayo College of Medicine, Mayo Clinic Hospital, Phoenix, Arizona, USA

Corresponding author: Mohamed Y Rady, editorial@ccforum.com

Critical Care 2005, **9**:170-176 (DOI 10.1186/cc2986)

Abstract

Over the past decade the practice of acute resuscitation and its monitoring have undergone significant changes. Utilization of noninvasive mechanical ventilation, goal-directed therapy, restricted fluid volume, blood transfusion and minimally invasive technology for monitoring tissue oxygenation have changed the practice of acute resuscitation. Early diagnosis and definitive treatment of the underlying cause of shock remains the mainstay for survival after successful resuscitation. Patient-centered outcome end-points, in addition to survival, are being utilized to appraise the effectiveness of treatment. Application of medical ethics to the ever changing practice of acute resuscitation has also become a societal expectation.

Introduction

Resuscitation from circulatory and respiratory failure represents the mainstay of emergency and critical care practice. Resuscitation alone will not ensure patient survival unless definitive treatment for the primary cause of the circulatory and/or respiratory failure is delivered in a timely manner. This review highlights some of the recent advances in the practice of resuscitation by emergency medicine physicians in the emergency department (ED). Advances in the resuscitation of cardiopulmonary arrest are not discussed here.

Diagnosis of life-threatening illness

Life-threatening illness can be defined as an acute illness for which delay or incorrect treatment will ultimately result in catastrophic morbidity or death. The commonest presentation is cardiovascular instability because the underlying illness has advanced to shock. Several types of shock have been described, based on the type of hemodynamic response (Table 1): cardiogenic, hypovolemic, obstructive, and distributive. Shock is characterized by inadequate tissue perfusion with an imbalance between tissue oxygen delivery and oxygen utilization, and cumulative build up of tissue hypoxia or oxygen debt. Oxygen debt is indicted by extracellular release of anaerobic metabolism products (e.g. lactic acid). Oxygen debt can result from a decrease in oxygen delivery and/or an increase in oxygen consumption, such as in hypovolemic, cardiogenic, or obstructive shock (Table 1). Under such conditions tissue oxygen extraction is increased, with simultaneous decrease in mixed venous oxygen saturation (SvO_2).

Distributive shock is characterized by impaired tissue oxygen extraction despite adequate or high systemic oxygen delivery (Table 1). Anaerobic metabolites (e.g. lactic acid) are released into the circulation in the face of a normal or elevated SvO_2, with a characteristic decrease in systemic oxygen extraction ratio. Other clinical presentations include acute respiratory and/or neurologic decompensation. Emergent interventions are necessary to stabilize vital organs and prevent further physiologic deterioration, which – without treatment – may culminate in cardiorespiratory arrest and death.

Although shock is an advanced manifestation that is common to a broad range of illnesses, it is essential that the underlying illness be determined and treated if a successful outcome from resuscitation is to be achieved. Mixed hemodynamic patterns are frequently seen in clinical practice, making classification of shock type to one of the aforementioned categories (Table 1) difficult. However, the resuscitation goals are the same, independent of the type of shock encountered: to restore systemic oxygen delivery, to normalize SvO_2, and to repay the incurred oxygen debt, with elimination of anaerobic metabolites.

Mode of resuscitation

The airway

Securing the airway remains the first and most important step in successful resuscitation, allowing supplemental oxygen to

---

CVP = central venous pressure; ED = emergency department; ICU = intensive care unit; PAC = pulmonary artery catheterization; PCO_2 = arterial carbon dioxide tension; $ScvO_2$ = central venous oxygen saturation; SvO_2 = mixed venous oxygen saturation.

Table 1

Classification of shock

	Type of shock			
Parameter(s)	Hypovolemic	Cardiogenic	Obstructive	Distributive
Preload, filling pressures, end-diastolic volumes	↓	↑	↕	↓
Pump, cardiac output	↓	↓	↓	↑
Afterload, systemic vascular resistance	↑	↑	↑	↓
Systemic oxygen delivery	↓	↓	↓	↑
Systemic oxygen consumption	↑	↓	↕	↕
Systemic oxygen extraction ratio	↑	↑	↑	↓
Global oxygen balance, $\mathrm{Sv}\mathrm{O}_2$ or $\mathrm{Scv}\mathrm{O}_2$	↓	↓	↓	↑

$\mathrm{Sv}\mathrm{O}_2$, mixed venous oxygen saturation; $\mathrm{Scv}\mathrm{O}_2$, central venous oxygen saturation.

be delivered. A variety of nasal, oral, and laryngeal devices are now available for use in difficult airways. The mainstay of securing the airway is still endotracheal intubation via either the nasal or oral route. Difficult intubation commonly arises because of poor glottic visualisation during laryngoscopy or high grade laryngeal view with inability to see the vocal cords. The use of sedative or muscle relaxant medications, especially those with a long duration of action, must be avoided if difficult intubation is anticipated. Blind nasal intubation during spontaneous breathing, laryngeal mask airway, intubating laryngeal mask airway, transtracheal needle jet ventilation, and fiberoptic bronchoscopy are among the airway rescue devices that are available under such circumstances [1]. Where there are anatomic or pathologic distortions to facial, cervical, or pharyngeal structures, a surgical airway with open or percutaneous cricothyroidotomy may be necessary for airway rescue. All clinicians should be familiar and experienced with at least one airway rescue technique in case of failed endotracheal intubation.

Mechanical ventilation

Assisted positive pressure ventilation (i.e. mechanical ventilation) may be necessary for delivering high inspired oxygen concentration and eliminating the work of breathing during resuscitation in the ED. Elimination of work of breathing can reduce systemic oxygen consumption and demands, with reversal of anaerobic metabolism and oxygen debt in shock.

Although invasive mechanical ventilation via endotracheal tube has been the main paradigm of emergency medicine practice over the past 2 decades, noninvasive mechanical ventilation has been proven to be a safe and effective alternative in certain clinical situations [2]. Noninvasive modes of mechanical ventilation with nasal, face, or helmet devices have successfully been used to stabilize patients with acute respiratory failure in the ED [3,4]. Both hypoxemic and hypercapnic acute respiratory failures have been shown to improve with noninvasive mechanical ventilation. Also, acute asthma, exacerbation of chronic obstructive pulmonary disease, congestive heart failure, and acute pulmonary edema can be effectively stabilized with noninvasive mechanical ventilation [5,6]. Advanced acute respiratory distress syndrome, altered level of consciousness, poor airway protection, and poor patient cooperation are contraindications to noninvasive mechanical ventilation because of high failure rate. Noninvasive modes of ventilation are advantageous because there is less morbidity from nosocomial pneumonia and shorter hospitalization as compared with invasive mechanical ventilation [7]. Furthermore, the frequency of other complications associated with barotrauma, the need for continuous sedation, and prolonged immobility are reduced by noninvasive positive pressure ventilation [8]. Appropriate patient selection, dedicated respiratory therapists, and established institutional guidelines will ensure successful application of noninvasive mechanical ventilation in acute respiratory failure [9].

Hemodynamic monitoring

Restoration of adequate global and tissue oxygenation remain the ‘gold standard’ markers for assessing the adequacy of resuscitation. A variety of strategies exist to assess circulatory status, including hemodynamic monitoring, tissue perfusion measurement, and use of anaerobic metabolism serum markers. There are several invasive and noninvasive methods available for monitoring hemodynamics (e.g. thermodilution pulmonary artery catheter, lithium dilution method, Doppler echocardiography, thoracic bioimpedance); these are discussed below. Although each method has distinct advantages, they also each have limitations, and it is important for the clinician to understand the strengths and limitations of the method employed in order to utilize the information derived to guide acute resuscitation effectively [10].

Invasive hemodynamic monitoring

Pulmonary artery catheterization (PAC) is the gold standard technique for invasive hemodynamic monitoring during acute resuscitation. Direct measurement of cardiac output, filling pressures, and $S\text{v}O_2$ can guide therapy to optimize cardiac function, normalize $S\text{v}O_2$, and restore the balance between systemic oxygen delivery and consumption. However, recent controlled studies have raised questions regarding the utility of PAC in the intensive care unit (ICU) setting because this type of monitoring does not translate into a decrease in mortality or morbidity as compared with conventional central venous catheterization [11,12]. It is uncertain whether the same conclusions can be drawn for the utility of PAC during acute resuscitation in the ED. The technical expertise required and demand imposed on nursing for this type of monitoring has limited its use in the ED setting.

A modified form of central venous catheterization has been developed to measure central venous pressure (CVP) and central venous oxygen saturation ($S\text{cv}O_2$) simultaneously during acute resuscitation in the ED [13,14]. Rivers and coworkers [13] conducted a trial of early goal-directed therapy, which included volume resuscitation with fluids to a CVP of 12 mmHg or higher, vasopressor infusion to restore mean arterial pressure to 65 mmHg or higher, followed by transfusion of packed red blood cells and/or dobutamine infusion to achieve a $S\text{cv}O_2$ of 70% or greater. Early goal-directed therapy restored systemic oxygen delivery with rapid elimination of anaerobic metabolites and decreased mortality from shock [13]. Therefore, ED resuscitation protocols that attempt to normalize CVP and $S\text{cv}O_2$ can improve global oxygenation and result in better survival.

Cardiac output can be measured continuously using the lithium dilution method and arterial waveform analysis [15,16]. The lithium dilution method requires central or peripheral intravenous infusion of lithium salt solution, followed by arterial sampling to measure stroke volume and cardiac output [17]. A small dose of lithium chloride is injected as an intravenous bolus, and cardiac output is derived from the dilution curve generated by a lithium-sensitive electrode attached to the arterial line. Analysis of arterial waveform energy provides a real-time calculation of stroke volume and cardiac output. This method can also be utilized with peripherally inserted central venous catheters in upper extremities, eliminating the hazards associated with central venous instrumentation. The lithium method has limitations when assessing low cardiac output states (e.g. hypovolemic or cardiogenic shock). However, in normal or high cardiac output states it can provide reliable information on stroke volume variation in real time, which can be difficult to obtain using traditional thermodilution methods.

Noninvasive hemodynamic monitoring

Doppler echocardiography, in the form of transthoracic or transesophageal echocardiography, permits intermittent or continuous noninvasive evaluation of hemodynamic parameters, including aortic blood flow, global and regional ventricular wall motion, and valvular integrity [18]. Cardiac output, preload, afterload, and contractility are measured or derived from the esophageal Doppler waveform. This method can yield valuable information regarding diastolic and systolic functions of left and right ventricles, as well as stroke volumes. However, the technology involved requires highly experienced operators for accurate image acquisition and interpretation in the ED. Cardiac output calculated from Doppler flow measurements require certain assumptions regarding the geometry and dimensions of cardiac chambers and thoracic aorta, which are age dependent.

Other noninvasive technologies such as thoracic bioimpedance for cardiac output determination are less operator dependent and can be applied in the ED. Measurements of stroke volume and cardiac output using the bioimpedance method can be influenced by rapid changes in extravascular and cellular fluid space content, especially during large volume resuscitation.

Tissue oxygenation monitoring

Metabolic acidosis and lactic acidosis are byproducts of anaerobic metabolism, and when they are measured in serum they can be useful markers of persistent tissue hypoxia or oxygen debt. Rapid bedside determination of blood lactate in the ED has been made feasible with newly developed enzymatic, substrate-specific electrodes [19]. A blood lactate of 4 mmol/l or higher is a useful triage test for detecting occult tissue hypoxia in the ED. Measurement of the elimination rate of an elevated lactate is also a valuable indicator of restoration of tissue oxygenation and relief from regional ischemia [13]. Delayed elimination of elevated lactate has been associated with subsequent development of multiple organ dysfunction and high mortality [20].

Gastric mucosa or sublingual partial carbon dioxide tension ($P\text{CO}_2$) can serve as a simple and noninvasive measurement for the diagnosis and estimation of the severity of shock in the ED. Gastric mucosal and sublingual $P\text{CO}_2$ are measured using tonometric catheters inserted into the stomach or beneath the tongue, respectively [21,22]. Gastric and sublingual $P\text{CO}_2$ are measured using automated devices; the device used to measure sublingual $P\text{CO}_2$ is a hand-held, portable device. A $P\text{CO}_2$ above 70 mmHg is associated with poor blood flow to the gastric or sublingual mucosa, and is consistent with global tissue ischemia [23]. The delayed response of mucosal $P\text{CO}_2$ to therapy limits its use for real-time monitoring of acute resuscitation.

Infrared and near infrared spectrometry, as is used in pulse oximetry, has been employed to monitor the oxidation-reduction state of hemoglobin and mitochondrial cytochrome *in vivo*. This type of technology provides noninvasive means for assessing cellular oxygenation and its recovery during acute resuscitation.

Transcutaneous oxygen and carbon dioxide electrodes have been used experimentally for early detection of tissue hypoxia and impending shock. However, the reproducibility of the clinical data, the real-time response, and associated background noise have been major obstacles to its wider application in clinical practice and use in the ED [24].

Fluid therapy

The mainstay of cardiovascular resuscitation is administration of intravenous fluids to increase circulating blood volume, cardiac preload, cardiac output, and systemic oxygen delivery. Current controversies remain focused on the type, composition, and volumes of fluid used during resuscitation [25]. Whether colloid or crystalloid should be used as the fluid of first choice remains uncertain because there is no difference in mortality between the two types of fluid [26]. A recent large randomized clinical trial comparing saline versus iso-oncotic human albumin solution for acute volume resuscitation has indicated that clinical outcome is similar with both fluid types [27].

Recently, renewed interest has focused on the use of small fluid volumes for acute resuscitation in uncontrolled hemorrhage and trauma, to avoid large increases in systolic arterial pressure and dilution of coagulation factors [28,29]. Hyper-osmolar sodium chloride (7%) and/or hyper-oncotic hydroxethyl starch (6%) have been utilized for small volume resuscitation safely in acute hypovolemic shock [30,31]. These types of fluids can maximally augment cardiac output at relatively small volumes and produce minimal hemodilution, while augmenting systemic oxygen delivery [32]. The type and volume of infused fluid can influence vascular endothelial integrity and capillary permeability [33]. Intra-abdominal compartment syndrome, intracranial hypertension, and pulmonary extravascular water accumulation are frequently associated with large fluid volume resuscitation. Compartment syndromes have deleterious effects on respiratory compliance, cardiovascular performance and splanchnic perfusion, and can precipitate multiple organ dysfunction [34,35]. Aggressive fluid resuscitation should focus on the use of efficient plasma volume expanders such as colloids and blood products in order to utilize the smallest volume of fluid needed to restore sufficient global and tissue oxygen delivery [36].

Blood transfusion

There has been growing concern regarding the relationship between blood transfusion and the incidence of nosocomial infections, organ dysfunction, and mortality in the critically ill. Restrictive transfusion practices and tolerance of anemia in a stable patient in the ICU was found more advantageous than transfusion practice aimed at a higher hemoglobin threshold in a randomized control trial [37,38]. Another observational study [39] reported that blood transfusion increased the risk for nosocomial infections and increased length of stay for patients in the ICU after adjustment for severity of illness at a single institution. However, no randomized control trials to date justify a change in the current transfusion practice of using either fresh or red cell concentrate of short shelf-life for augmenting oxygen delivery and avoiding the deleterious effects of high doses of vasopressor and/or inotropic drugs for cardiovascular support during resuscitation.

Cardiovascular support

Cardiovascular support during resuscitation may require administration of pharmacologic vasoactive agents with vasopressor and/or inotropic actions after blood volume is restored [40]. Physiologic end-points of global and regional oxygenation should be used for titration of vasoactive drugs (Table 2) to avoid deleterious effects from their inappropriate or excessive use [41]. Venous oxygen saturation (either $\mathrm{Sv}O_2$ or $\mathrm{Scv}O_2$), plasma or blood lactate clearance rate, sublingual or gastric mucosal $\mathrm{P}CO_2$, and urinary output are useful parameters for assessing the effectiveness of pharmacologic interventions. Temporary mechanical support with an intra-aortic balloon pump may be necessary in cardiogenic shock associated with acute coronary syndrome.

Definitive treatment

Although initial resuscitation will stabilize vital organs and restore visceral perfusion and oxygenation, early definitive treatment of the underlying cause of illness is required to ensure survival. In penetrating and blunt trauma, certain clinical indications require emergent surgical intervention. Interventional revascularization in acute coronary syndrome has been shown to improve survival from cardiogenic shock secondary to acute coronary syndrome. Percutaneous drainage, arterial or venous embolization, and insertion of intraluminal stents or filters with the assistance of interventional radiology can eliminate the need for surgical intervention in certain situations [42,43].

Appropriate antimicrobial therapy and early intervention to control sources of infection are the main pillars of definitive treatment for sepsis [44]. Activated protein C can be given in septic shock when cardiovascular dysfunction and/or pulmonary dysfunction are established in order to reduce mortality. Corticosteroid replacement for adrenal insufficiency had been shown to improve cardiovascular stability and perhaps decrease mortality in septic shock.

Outcomes of resuscitation

The success of resuscitation and treatment is commonly measured in terms of 28-day or hospital survival. Unfortunately, for many patients and families, survival is unacceptable if it is associated with catastrophic morbidity, such as care dependency or cognitive, psychological, and/or physical disability [45]. A refocusing on patient-centered outcomes that are meaningful to patients and families is essential in measuring the success of resuscitation and treatment [46]. Several factors are known to influence

Table 2

Common vasoactive agents used for cardiovascular support during resuscitation

Type of action	Drugs
Inotropic	Dobutamine
	Milrinone
	Dopexamine
Combined	Dopamine
	Epinephrine
Vasomotor	Norepinephrine
	Phenylephrine
	Vasopressin

Table 3

Outcome of resuscitation

Outcome end-points	Factors that impact on outcome
28-day survival	Age
Hospital survival	Pre-illness function and mobility
Long term care dependency	Chronic end-stage organ disease
Return to independent function	Etiology of acute illness
Quality of life-adjusted survival	Timing of resuscitation and definitive treatment

resuscitation outcomes (Table 3). Adequacy and timing of acute resuscitation, as well as definitive treatment of the underlying illness, will influence short-term outcomes such as incidence of multiple organ failure and hospital survival [47]. However, short-term outcomes do not always reflect pertinent long-term outcomes such as physical, cognitive, or psychological functioning, and subsequent life span. Long-term consequences may be attributed to the precipitating illness, resuscitation, or definitive treatment, or all of these combined. Advanced age, debilitation, impaired pre-illness functional status, chronic disease, genotype, and socio-economic environment can also predispose to long-term sequelae on survival.

Ethical considerations in resuscitation

A recent epidemiologic survey [48] indicated that intensive care is used in one out of five deaths in the USA, raising significant concerns regarding the appropriateness of the type of care offered to terminally ill, hospitalized patients. That survey emphasizes the importance of informed participation of patients and surrogates in decision making regarding resuscitation and life-sustaining therapy. Physicians are obliged to preserve the principles of beneficence, non-maleficence, and respect for patient autonomy under all circumstances, including during acute resuscitation [49]. However, the urgency of acute resuscitation and the impaired ability of the patient to make a reasonable autonomous decision both conspire against adequate consideration of the principles of medical ethics.

Health care providers often make initial resuscitation decisions unilaterally. Under such circumstances, gaining informed consent is not feasible and may lead to a common misconception that consent is not required for resuscitation, because it brings benefit and prevents harm, and the patient is unable to give or withhold consent. Physicians who are engaged in acute resuscitation have professional obligations to address certain ethical issues. First, did the patient or their surrogate participate in an informed decision making process? Second, will treatment confer survival, restore functional independence, and improve the patient's quality of life? Third, will treatment result in short-term or long-term complications, disability, and/or care dependency? Finally, will treatment represent efficient utilization of limited health care resources?

Information gathered from advanced directives, living wills, and family discussions that indicate patient-expressed attitudes or wishes regarding such a situation must be considered, along with the likely benefits and harms of the resuscitation endeavor. The physician responsible for initiating resuscitation or life-sustaining therapy must fulfill that task [50]. Life-sustaining therapy that simply delays death and prolongs suffering is unacceptable, and should be carefully reconsidered. Medical futility of resuscitation because of long-term permanent disability and poor quality of life must be addressed in each clinical situation with surrogate decision makers [51].

Conclusion

The modes and methods for monitoring acute resuscitation have undergone significant changes over the past decade. Patient-centered outcome measures and observance of ethical principles are becoming integral to the everyday practice of resuscitation.

Competing interests

The author has no affiliations or financial involvement with any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript.

References

1. Orebaugh SL: **Difficult airway management in the emergency department.** *J Emerg Med* 2002, **22:**31-48.
2. Sigillito RJ, DeBlieux PM: **Evaluation and initial management of the patient in respiratory distress.** *Emerg Med Clin North Am* 2003, **21:**239-258.
3. Murray S: **Bi-level positive airway pressure (BiPAP) and acute cardiogenic pulmonary oedema (ACPO) in the emergency department.** *Aust Crit Care* 2002, **15:**51-63.

4. Pelosi P, Severgnini P, Aspesi M, Gamberoni C, Chiumello D, Fachinetti C, Introzzi L, Antonelli M, Chiaranda M: **Non-invasive ventilation delivered by conventional interfaces and helmet in the emergency department.** *Eur J Emerg Med* 2003, **10:**79-86.
5. Lightowler JV, Wedzicha JA, Elliott MW, Ram FS: **Non-invasive positive pressure ventilation to treat respiratory failure resulting from exacerbations of chronic obstructive pulmonary disease: Cochrane systematic review and meta-analysis.** *BMJ* 2003, **326:**185.
6. L'Her E: **Noninvasive mechanical ventilation in acute cardiogenic pulmonary edema.** *Curr Opin Crit Care* 2003, **9:**67-71.
7. Gali B, Goyal DG: **Positive pressure mechanical ventilation.** *Emerg Med Clin North Am.* 2003, **21:**453-473.
8. Ram FS, Lightowler JV, Wedzicha JA: **Non-invasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease.** *Cochrane Database Syst Rev* 2003, **1:**CD004104.
9. Sinuff T, Cook DJ, Randall J, Allen CJ: **Evaluation of a practice guideline for noninvasive positive-pressure ventilation for acute respiratory failure.** *Chest* 2003, **123:**2062-2073.
10. Chaney JC, Derdak S: **Minimally invasive hemodynamic monitoring for the intensivist: current and emerging technology.** *Crit Care Med* 2002, **30:**2338-2345.
11. Rhodes A, Cusack RJ, Newman PJ, Grounds RM, Bennett ED: **A randomised, controlled trial of the pulmonary artery catheter in critically ill patients.** *Intensive Care Med* 2002, **28:**256-264.
12. Richard C, Warszawski J, Anguel N, Deye N, Combes A, Barnoud D, Boulain T, Lefort Y, Fartoukh M, Baud F, *et al.*: **Early use of the pulmonary artery catheter and outcomes in patients with shock and acute respiratory distress syndrome: a randomized controlled trial.** *JAMA* 2003, **290:**2713-2720.
13. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M; Early Goal-Directed Therapy Collaborative Group: **Early goal-directed therapy in the treatment of severe sepsis and septic shock.** *N Engl J Med* 2001, **345:**1368-1377.
14. Ladakis C, Myrianthefs P, Karabinis A, Karatzas G, Dosios T, Fildissis G, Gogas J, Baltopoulos G: **Central venous and mixed venous oxygen saturation in critically ill patients.** *Respiration* 2001, **68:**279-285.
15. Hamilton TT, Huber LM, Jessen ME: **PulseCO: a less-invasive method to monitor cardiac output from arterial pressure after cardiac surgery.** *Ann Thorac Surg* 2002, **74:**S1408-S1412.
16. Cottis R, Magee N, Higgins DJ: **Haemodynamic monitoring with pulse-induced contour cardiac output (PiCCO) in critical care.** *Intensive Crit Care Nurs* 2003, **19:**301-307.
17. Jonas MM, Tanser SJ: **Lithium dilution measurement of cardiac output and arterial pulse waveform analysis: an indicator dilution calibrated beat-by-beat system for continuous estimation of cardiac output.** *Curr Opin Crit Care* 2002, **8:**257-261.
18. Axler O, Megarbane B, Lentschener C, Fernandez H: **Comparison of cardiac output measured with echocardiographic volumes and aortic Doppler methods during mechanical ventilation.** *Intensive Care Med* 2003, **29:**208-217.
19. Aduen J, Bernstein WK, Khastgir T, Miller J, Kerzner R, Bhatiani A, Lustgarten J, Bassin AS, Davison L, Chernow B: **The use and clinical importance of a substrate-specific electrode for rapid determination of blood lactate concentrations.** *JAMA* 1994, **272:**1678-1685.
20. Husain FA, Martin MJ, Mullenix PS, Steele SR, Elliott DC: **Serum lactate and base deficit as predictors of mortality and morbidity.** *Am J Surg* 2003, **185:**485-491.
21. Rackow EC, O'Neil P, Astiz ME, Carpati CM: **Sublingual capnometry and indexes of tissue perfusion in patients with circulatory failure.** *Chest* 2001, **120:**1633-1638.
22. Boswell SA, Scalea TM: **Sublingual capnometry: an alternative to gastric tonometry for the management of shock resuscitation.** *AACN Clin Issues* 2003, **14:**176-184.
23. Weil MH, Nakagawa Y, Tang W, Sato Y, Ercoli F, Finegan R, Grayman G, Bisera J: **Sublingual capnometry: a new noninvasive measurement for diagnosis and quantitation of severity of circulatory shock.** *Crit Care Med* 1999,**27:**1225-1229.
24. Tatevossian RG, Wo CC, Velmahos GC, Demetriades D, Shoemaker WC: **Transcutaneous oxygen and CO2 as early warning of tissue hypoxia and hemodynamic shock in critically ill emergency patients.** *Crit Care Med* 2000, **28:**2248-2253.
25. Bradley C: **Crystalloid, colloid or small volume resuscitation?** *Intensive Crit Care Nurs* 2001, **17:**304-306.
26. Rizoli SB: **Crystalloids and colloids in trauma resuscitation: a brief overview of the current debate.** *J Trauma* 2003, **Suppl:**S82-S88.
27. The SAFE Study Investigators: **A comparison of albumin and saline for fluid resuscitation in the intensive care unit.** *N Engl J Med* 2004, **350:**2247-2256.
28. Dutton RP, Mackenzie CF, Scalea TM: **Hypotensive resuscitation during active hemorrhage: impact on in-hospital mortality.** *J Trauma* 2002, **52:**1141-1146.
29. Revell M, Greaves I, Porter K: **Endpoints for fluid resuscitation in hemorrhagic shock.** *J Trauma* 2003, **Suppl:**S63-S67.
30. Oliveira RP, Velasco I, Soriano F, Friedman G: **Clinical review: Hypertonic saline resuscitation in sepsis.** *Crit Care* 2002, **6:** 418-423.
31. Freudenberg S, Palma P, Schuster K, Mkony C, Waschke K: **Small volume resuscitation with 7.5% hypertonic saline solution: treatment of haemorrhagic shock in the tropics.** *Trop Doct.* 2003, **33:**165-166.
32. Mauritz W, Schimetta W, Oberreither S, Polz W: **Are hypertonic hyperoncotic solutions safe for prehospital small-volume resuscitation? Results of a prospective observational study.** *Eur J Emerg Med* 2002, **9:**315-319.
33. Jaeger K, Heine J, Ruschulte H, Juttner B, Scheinichen D, Kuse ER, Piepenbrock S: **Effects of colloidal resuscitation fluids on the neutrophil respiratory burst.** *Transfusion* 2001, **41:**1064-1068.
34. Biffl WL, Moore EE, Burch JM, Offner PJ, Franciose RJ, Johnson JL: **Secondary abdominal compartment syndrome is a highly lethal event.** *Am J Surg* 2001, **182:**645-648.
35. Balogh Z, McKinley BA, Cocanour CS, Kozar RA, Valdivia A, Sailors RM, Moore FA: **Supranormal trauma resuscitation causes more cases of abdominal compartment syndrome.** *Arch Surg* 2003, **138:**637-642; discussion 642-633.
36. Wu JJ, Huang MS, Tang GJ, Kao WF, Shih HC, Su CH, Lee CH: **Hemodynamic response of modified fluid gelatin compared with lactated ringer's solution for volume expansion in emergency resuscitation of hypovolemic shock patients: preliminary report of a prospective, randomized trial.** *World J Surg* 2001, **25:**598-602.
37. Hebert PC, Wells G, Martin C, Tweeddale M, Marshall J, Blajchman M, Pagliarello G, Schweitzer I, Calder L: **A Canadian survey of transfusion practices in critically ill patients. Transfusion Requirements in Critical Care Investigators and the Canadian Critical Care Trials Group.** *Crit Care Med.* 1998, **26:**482-487.
38. Hebert PC, Yetisir E, Martin C, Blajchman MA, Wells G, Marshall J, Tweeddale M, Pagliarello G, Schweitzer I; Transfusion Requirements in Critical Care Investigators for the Canadian Critical Care Trials Group: **Is a low transfusion threshold safe in critically ill patients with cardiovascular diseases?** *Crit Care Med* 2001, **29:**227-234.
39. Taylor RW, Manganaro L, O'Brien J, Trottier SJ, Parkar N, Veremakis C: **Impact of allogenic packed red blood cell transfusion on nosocomial infection rates in the critically ill patient.** *Crit Care Med* 2002, **30:**2249-2254.
40. Ruokonen E, Parviainen I, Uusaro A: **Treatment of impaired perfusion in septic shock.** *Ann Med* 2002, **34:**590-597.
41. Trager K, DeBacker D, Radermacher P: **Metabolic alterations in sepsis and vasoactive drug-related metabolic effects.** *Curr Opin Crit Care* 2003, **9:**271-278.
42. Ajani AE, Maruff P, Warren R, Eccleston D, Dick R, MacIsaac A, Rowe M, Lefkovits J: **Impact of early percutaneous coronary intervention on short- and long-term outcomes in patients with cardiogenic shock after acute myocardial infarction.** *Am J Cardiol* 2001, **87:**633-635, A639-A610.
43. Kushimoto S, Arai M, Aiboshi J, Harada N, Tosaka N, Koido Y, Yoshida R, Yamamoto Y, Kumazaki T: **The role of interventional radiology in patients requiring damage control laparotomy.** *J Trauma* 2003, **54:**171-176.
44. Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, Gea-Banacloche J, Keh D, Marshall JC, Parker MM, *et al.*: **Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock.** *Crit Care Med* 2004, **32:**858-873.
45. Buckley TA, Cheng AY, Gomersall CD: **Quality of life in long-term survivors of intensive care.** *Ann Acad Med Singapore* 2001, **30:**287-292.
46. Angus DC, Carlet J; 2002 Brussels Roundtable Participants: **Surviving intensive care: a report from the 2002 Brussels Roundtable.** *Intensive Care Med* 2003, **29:**368-377.

47. Gallagher SF, Williams B, Gomez C, DesJardins C, Swan S, Durham RM, Flint LM: **The role of cardiac morbidity in short- and long-term mortality in injured older patients who survive initial resuscitation.** *Am J Surg* 2003, **185:**131-134.
48. Angus DC, Barnato AE, Linde-Zwirble WT, Weissfeld LA, Watson RS, Rickert T, Rubenfeld GD; Robert Wood Johnson Foundation ICU End-Of-Life Peer Group: **Use of intensive care at the end of life in the United States: an epidemiologic study.** *Crit Care Med* 2004, **32:**638-643.
49. Berger JT: **Ethical challenges of partial do-not-resuscitate (DNR) orders: placing DNR orders in the context of a life-threatening conditions care plan.** *Arch Intern Med* 2003, **163:** 2270-2275.
50. Ardagh M: **Resurrecting autonomy during resuscitation: the concept of professional substituted judgment.** *J Med Ethics* 1999, **25:**375-378.
51. Hook CC, Koch KA: **Ethics of resuscitation.** *Crit Care Clin* 1996, **12:**135-148.