Epidemiology of Sepsis in Surgical Patients

Laura J. Moore, MD, a, *, Frederick A. Moore, MD b

INTRODUCTION

Despite advances in surgical critical care, sepsis among surgical patients continues to be a common and serious problem. As the population ages, the incidence of sepsis in the United States continues to rise. It is estimated that in the United States, there are greater than 1.1 million cases of sepsis per year at an annual cost of $24.3 billion. Sepsis remains the leading cause of death in noncardiac ICUs. In spite of extensive research, sepsis-related mortality remains prohibitively high (>40%).

Among surgical patients, sepsis is a leading cause of morbidity and mortality. Surgical patients account for nearly one-third of sepsis cases in the United States. A recent analysis of the American College of Surgeons National Surgical Quality Improvement Project Database determined that sepsis and septic shock are 10 times more common than perioperative myocardial infarction and pulmonary embolism. In addition, the mortality rate for septic shock in the perioperative period exceeds that of both myocardial infarction and pulmonary embolism. These findings underscore the importance of studying sepsis specifically in general surgery patients.

Risk factors for both the development of sepsis and death from sepsis included age older than 60 years, the need for emergency surgery, and the presence of comorbid...
Intraabdominal infection is the most common source of sepsis among surgical patients, accounting for approximately two-thirds of all cases. Among intraabdominal causes of sepsis, colon perforation is the predominant source of intraabdominal sepsis. When septic shock follows sepsis, there is a 39% mortality rate among emergent surgical patients and a 30% mortality rate among elective surgical patients.

DEFINITION OF SURGICAL SEPSIS

A clear and accurate definition of surgical sepsis is critical for clinicians and researchers. Standard definitions allow us to identify patients, lead to a better understanding of the disease process, and facilitate clinical research. Roger Bone first defined the sepsis syndrome in the literature in 1989. This was followed by the American College of Chest Physicians and the Society of Critical Care Medicines (ACCP/SCCM) Consensus Conference in 1991 that defined the systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndrome (MODS). A second consensus conference was convened in 2001 to revise the original definitions. The updated consensus conference definitions expanded the list of signs and symptoms of sepsis. Although the 2001 definitions are widely accepted, they do not specifically define surgical sepsis. The consensus conference definitions remain nonspecific and allow variability, especially in defining organ dysfunction.

In an attempt to better define the categories of sepsis, severe sepsis, and septic shock the authors have modified the ACCP/SCCM Consensus Conference definitions. The modified definition of surgical sepsis is SIRS plus an infection requiring surgical intervention for source control or SIRS plus an infection within 14 days of a major surgical procedure. A major surgical procedure is defined as any procedure requiring general anesthesia for more than 1 hour. Severe sepsis is defined as SIRS plus infection plus acute organ dysfunction. The types of acute organ dysfunction are further defined. Neurologic is identified as a Glasgow Coma Scale (GCS) less than 13 on recognition of sepsis or deteriorating GCS during the first 24 hours. Pulmonary dysfunction includes a PaO2 to fraction of inspired oxygen ratio less than 250 (<200 if lung is primary site of infection) and pulmonary capillary wedge pressure (PCWP), if available, not suggestive of fluid overload. Renal dysfunction is defined as one of the following criteria: (1) urine output less than 0.5 mL/kg for greater than or equal to 1 hour despite adequate volume resuscitation, (2) increase in serum creatinine greater than or equal to 0.5 mg/dL from baseline (measured within 24 hrs of starting sepsis resuscitation) despite adequate volume resuscitation, or (3) increase in serum creatinine greater than or equal to 0.5 mg/dL during first 24 hours of sepsis management despite adequate volume resuscitation. Adequate volume resuscitation is defined as a minimum intravenous (IV) fluid infusion of 20 mL/kg of ideal body weight or central venous pressure (CVP) greater than or equal to 8 mm Hg or PCWP greater than or equal to 12 mm Hg. Coagulation dysfunction is also described by any one of these criteria: international normalized ratio greater than 1.5, platelet count less than 80,000 or greater than or equal to 50%, or decreased platelets compared with 24 hours before instituting sepsis resuscitation or in the 24 hours after starting sepsis resuscitation in the absence of chronic liver disease. Hypoperfusion is defined by a lactate level greater than 4 mmol/L. Cardiac dysfunction is defined by the presence of an IV fluid challenge greater than or equal to 20 mL/kg of ideal body weight of isotonic crystalloid infusion, CVP greater than or equal to 8 mm Hg, or PCWP greater than or equal to 12 mm Hg and the requirement for vasopressors to increase mean arterial pressure (MAP) greater than or equal to 65 mm Hg. Septic shock is defined as SIRS plus infection plus acute cardiac dysfunction.
SEPSIS SCREENING

The early identification and management of sepsis remains a significant challenge to health care providers. Multiple organizations have focused their efforts on providing evidence-based guidelines (EBGs) in an attempt to decrease the morbidity and mortality associated with sepsis. Identifying patients in the early stages of sepsis is imperative if mortality rates are to be improved. If patients are allowed to progress from sepsis into septic shock, their mortality is prohibitively high (>40%) despite aggressive interventions. The interventions demonstrated to improve survival in patients with sepsis are time-sensitive. The use of early goal-directed therapy (EGDT) for patients with severe sepsis and septic shock improves survival rates. Administration of empiric, broad-spectrum, antibiotic therapy is recommended within 1 hour of recognition of sepsis-induced hypotension. Each hour of delay in the administration of antibiotic therapy is associated with an increased mortality rate. However, early intervention requires early identification of sepsis. A recently published study by Kumar and colleagues demonstrated a significant correlation between time to appropriate antibiotic administration and patient survival.

In spite of strong evidence that the early implementation of evidence-based, sepsis-specific therapies saves lives, the early identification of sepsis remains challenging. The signs and symptoms of sepsis are nonspecific, particularly in the early phases of sepsis. Because health care providers focus on multiple priorities and tasks, early signs of sepsis are often missed, resulting in delays for the time-sensitive interventions that improve patient outcomes. In the surgical patient, some of the early signs of sepsis are often attributed to other common problems seen in the postoperative period. For example, altered mental status is often attributed to the administration of narcotic pain medication or sundowning, particularly in the elderly patient. Oliguria is often attributed to underresuscitation. Although many nurses notify physicians of hyperthermia, hypothermia, which is also an early sign of sepsis, is often not reported. Likewise, acute hypoxia on the surgical wards spurs a workup for pulmonary embolism. However, it may also herald the onset of severe sepsis or septic shock. Identifying patients in these early stages of sepsis is imperative. Considering these factors, the benefit of routine, accurate screening of patients for sepsis quickly becomes apparent.

An audit of ward nurses demonstrated that fewer than 40% were able to recognize a patient with sepsis. Physicians also struggle with the early identification and evidence-based management of sepsis. A recent survey of 917 physicians showed that only 27.3% of physicians were able to recognize sepsis. Recognition of severe sepsis and septic shock was slightly improved, but still unsatisfactory, at 56.7% and 81%, respectively. The reasons listed for missing the diagnosis of sepsis included lack of monitoring, lack of a common definition for sepsis, and lack of knowledge. Of the 1058 physicians surveyed, only 140 (13.2%) were able to give the definition of sepsis from the ACCP/SCCM Consensus Conference statement. These results are confirmed in other studies reporting similar findings.

Little attention has been dedicated to the topic of sepsis screening. The use of SIRS score to identify patients with sepsis has been largely abandoned because of lack of sensitivity and specificity. The Early Warning Score and Modified Early Warning Score can predict illness severity and in-hospital mortality but are not helpful in the early recognition of sepsis. Attempting to increase the early identification of sepsis, a sepsis screening tool was developed at the author’s Surgical Intensive Care Unit (SICU). The initial portion of this sepsis screening tool (Fig. 1) focuses on assessing SIRS severity and is completed by the bedside nurse. A score of greater
than or equal to 4 is considered to be a positive score and prompts the nurse to call a clinician to evaluate the patient for a possible infection (Fig. 2). Initial experience with this mandatory sepsis screening tool in the SICU showed promising results. The screening tool yielded a sensitivity of 96.5%, a specificity of 96.7%, a positive predictive value of 80.2%, and a negative predictive value of 99.5%. In addition, sepsis-related mortality decreased from 35.1% to 23.3%. Subsequently, the institution has implemented and validated the sepsis screening tool on the inpatient surgical ward. The screening tool yielded a sensitivity of 99.9%, specificity of 91.3%, a positive predictive value of 16.3%, and a negative predictive value of 99.9%. The sepsis-related mortality in those patients who screened positive for sepsis was 6.3%. Subsequent implementation and validation of this sepsis screening tool among trauma patients yielded similar results with a sensitivity of 97.9%, specificity of 91.8%, positive predictive value of 51%, and negative predictive value of 99.8%. It is important to emphasize the extremely high negative predictive value (99.5%–99.9%) of this sepsis screening tool across a broad range of surgical patients. These results emphasize the importance of sepsis screening for the early identification of sepsis.

**PRACTICAL CONSIDERATIONS FOR THE MANAGEMENT OF SURGICAL SEPSIS**

**Initial Assessment**

A clinical suspicion of sepsis should prompt further evaluation of the patient. This initial evaluation should focus on determining the degree of physiologic derangement exhibited by the patient. It is especially important to assess for the presence and
The degree of tissue hypoperfusion. There are several clinical and laboratory variables that can be used to evaluate the state of tissue perfusion. The following indicate that the patient is experiencing tissue hypoperfusion: (1) urine output less than 0.5 mL/kg of ideal body weight, (2) MAP less than 65 mm Hg, (3) GCS less than 12, and (4) serum lactate greater than or equal to 4 mmol/L. Tissue hypoperfusion should prompt aggressive resuscitative measures focused on restoring tissue perfusion. Patients who do not have evidence of tissue hypoperfusion fall into the category of sepsis using current definitions. Patients who do have evidence of tissue hypoperfusion are categorized as having severe sepsis and/or septic shock.

**Initial Resuscitation of Sepsis**

The initial resuscitation phase begins immediately on recognition of sepsis. Initiation of resuscitation should not wait until the patient is transferred to a higher level of care.
The goals of the resuscitation include restoration of intravascular volume, diagnosis of the source of infection, initiation of broad spectrum antimicrobial therapy, and source control. Many institutions have developed sepsis order sets that specifically address each of these issues. The use of standardized protocols for the initial management of sepsis improves patient outcomes in multiple settings.7,23–27

The major tenets of initial resuscitation can be initiated in any area of the hospital and should not be delayed pending transfer to the ICU. Establishing IV access is a critical first step because this allows for the administration of resuscitative IV fluid and antimicrobials. For those patients without evidence of tissue hypoperfusion, a large-bore peripheral IV should be sufficient. If peripheral IV access is not attainable, a large-bore central venous line should be inserted in a timely fashion to facilitate fluid resuscitation.

Fluid resuscitation should be guided with the following goals in mind: (1) CVP, if available, 8 to 12 mm Hg in nonintubated patients and a target CVP 12 to 15 mm Hg in mechanically ventilated patients,28 (2) MAP greater than or equal to 65 mm Hg,29 (3) urine output greater than or equal to 0.5 mL/kg/h, and (4) central venous oxygen saturation (ScvO2) greater than or equal to 70% or mixed venous oxygen saturation (SvO2), if available, greater than or equal to 65%.11 These endpoints of resuscitation should be achieved within 6 hours of the recognition of sepsis. In addition, a baseline serum lactate is sent on the identification of sepsis. A repeat serum lactate level is sent 4 hours later to monitor the progress of the initial resuscitation.

The initial resuscitation fluid of choice remains extremely controversial. There are no prospective, randomized, controlled trials evaluating crystalloid versus colloid resuscitation in surgical patients with sepsis. If colloids are given, the initial fluid bolus should be 300 to 500 mL of colloid over 30 minutes. If crystalloids are given, the initial fluid challenge should be 1000 cc of crystalloid over 30 minutes. The patient’s response to fluid bolus will dictate the need for additional resuscitation. The Saline versus Albumin Fluid Evaluation (SAFE) study randomized nearly 7000 critically ill patients requiring fluid resuscitation to receive albumin or normal saline and no difference in mortality was identified. Interestingly, a subgroup analysis of the 1218 patients with severe sepsis documented that albumin was associated with a trend toward reduced mortality (relative risk of death 0.87; 95% CI 0.74–1.02).30 Currently, two randomized trials are ongoing to investigate this finding. They are, in Italy, the Volume Replacement with Albumin in Severe Sepsis (ALBIOS) trial31 and, in France, the Early Albumin Resuscitation during Septic Shock trial.32

Initial Resuscitation of Severe Sepsis and Septic Shock

For patients presenting with severe sepsis and septic shock, the timely correction of tissue hypoperfusion is critical. The concept of EGDT in severe sepsis and septic shock was initially developed and validated in the emergency department (ED) setting in a single-center trial.11 The ED is frequently the point of entry for many septic patients into the hospital. Unfortunately, many of these patients may wait for prolonged periods of time in the ED. The end result is often a delay in the implementation of early sepsis resuscitation.

The implementation of EGDT improves survival in patients presenting with severe sepsis and septic shock.11,26,33,34 The basic principles of EGDT are to recognize tissue hypoperfusion and initiate therapies to reverse global tissue hypoxia by optimizing oxygen delivery. Tissue perfusion can be monitored by measuring SvO2, ScvO2, or peripheral muscle hemoglobin oxygen saturation (StO2). A SvO2 of less than or equal to 65%, a ScvO2 of less than or equal to 70%, or a StO2 of less than or equal to 75% are considered indicators of tissue hypoperfusion. Once tissue hypoperfusion is
identified, specific therapies are instituted to reverse tissue hypoxia by restoring adequate perfusion. The factors affecting oxygen delivery are cardiac output, hemoglobin, and percent arterial hemoglobin oxygen saturation (SaO2). EGDT attempts to restore tissue perfusion by addressing these variables. The evidence-based Sepsis Resuscitation Bundle (SRB) was established with a goal to accomplish all indicated tasks, 100% of the time, within 6 hours of the diagnosis of sepsis. The elements of the 6 hour SRB include measurement of serum lactate, obtaining blood cultures before the initiation of antibiotics, administration of broad-spectrum antibiotics within 1 hour of sepsis recognition, and fluid resuscitation for the treatment of hypotension.

To restore intravascular volume and enhance cardiac output, an initial crystalloid fluid bolus of 20 mL/kg of ideal body weight is recommended. This fluid bolus can be administered initially through existing peripheral IVs; however, placement of a central venous line for monitoring of CVP is recommended. An arterial line should be placed in patients with unresponsive hypotension. The use of noninvasive blood pressure monitoring for patients in septic shock often produces inaccurate measurements and should be avoided for titration of vasoactive medications. A Foley catheter is inserted to allow for close monitoring of urine output. Bladder pressures should be monitored in patients requiring aggressive volume loading to recognize abdominal compartment syndrome (ACS). The goals of resuscitation remain the same as those listed above. In the event that a ScvO2 of greater than or equal to 70% or SvO2 greater than or equal to 65% cannot be achieved with restoration of intravascular volume and MAP of 65 to 90 mm Hg, red blood cells should be transfused to achieve of hematocrit of greater than or equal to 30%.

Multiple international randomized controlled trials of early goal-directed therapy for patients with severe sepsis are underway to validate the findings of the single-center Rivers trial. These include ProCESS (Protocolized Care for Early Septic Shock), ARISE (Australian Resuscitation in Sepsis Evaluation), and ProMISe (Protocolized Management in Sepsis). The ProCESS trial will randomize 1950 subjects who present to the ED in septic shock to three arms: (1) the EGDT Rivers protocol described above, (2) a less complicated, less invasive protocol using esophageal Doppler monitor and no blood transfusion, and (3) usual care. The ARISE trial will randomize 1600 subjects to EGDT versus standard care and assess 90-day mortality in subjects presenting to the ED with severe sepsis. The ProMISe trial will randomize 1260 subjects to EGDT versus standard care and assess 90-day mortality in subjects presenting to the ED with septic shock. Furthermore, an individual, subject data meta-analysis will be performed across the three trials.

Having achieved the goal CVP, the goal MAP, and the goal hematocrit, if there is still evidence of tissue hypoperfusion, inotropic agents should be administered to improve cardiac output. In patients presenting with septic shock, the initial fluid bolus may not restore their MAP to greater than or equal to 65 mm Hg. A repeat fluid bolus of 20 mL/kg of ideal body weight can be given to correct hypovolemia. However, transient vasopressors therapy may need to be initiated, even if volume resuscitation is still ongoing.

Vasopressor therapy

Septic shock is primarily a vasodilatory shock, associated with a high cardiac output and a low systemic vascular resistance. Therefore, initial vasopressors therapy should be targeted at restoring vascular tone. Both norepinephrine and dopamine are acceptable first-line agents for treatment of septic shock, and should be administered through a central venous catheter. Norepinephrine is primarily an α-receptor agonist that promotes widespread vasoconstriction and has little effect on heart rate or stroke volume. Dopamine has dose-dependent effects on α-, β-, and dopaminergic...
receptors. The initial increase in blood pressure seen with dopamine is related to increasing cardiac output. At higher doses (>7.5 μg/kg/min), dopamine does activate \( \alpha \)-receptors with resultant vasoconstriction.

In patients with septic shock that is refractory to first-line vasopressors, the addition of vasopressin may be beneficial. Vasopressin is a stress hormone that has vasoactive effects. The use of vasopressin is supported by suggestive data indicating that in states of septic shock there is a relative deficiency of vasopressin. The administration of vasopressin in this patient population improves responsiveness to catecholamines and potentially reduces the amount of catecholamine needed to maintain blood pressure.

The Vasopressin and Septic Shock Trial (VASST) randomized 779 subjects in septic shock requiring norepinephrine (5 μg/min) for at least 6 hours and at least one organ system dysfunction present for less than 24 hours to vasopressin (0.01–0.03 U/min) versus higher dose norepinephrine (5–15 μg/min). No difference in 28-day or 90-day mortality was identified. In the prospectively defined stratum of less severe septic shock, the mortality rate was lower in the vasopressin group than in the norepinephrine group at 28 days (26.5% vs 35.7%, \( P = .05 \)) which persisted to 90-day mortality (35.8% vs 46.1%, \( P = .04 \)). A post hoc analysis of the VASST study identified that the combination of low-dose vasopressin and corticosteroids was associated with decreased mortality and organ dysfunction compared with norepinephrine and corticosteroids. Based on the results of studies to date, clinicians should consider the addition of low-dose continuous infusion vasopressin (up to 0.03 U/min) in individual septic shock patients who, despite adequate resuscitation, are still requiring high doses of vasopressors. It is the author’s current practice to initiate a vasopressin drip at a rate of 0.04 U/min in patients requiring norepinephrine infusion at greater than or equal to 15 μg/min. The dose of vasopressin should not exceed 0.04 U/min because of the possibility of decreased cardiac output and myocardial ischemia at higher doses.

Although most patients with sepsis initially present with increased cardiac output, a subset of patients will develop myocardial depression from sepsis. The exact mechanism for this reversible myocardial dysfunction is still under investigation. B-type natriuretic peptide (BNP) is secreted in response to stretching of myocardium and is used clinically to assess volume overload and predict death in acute congestive heart failure. BNP is elevated in early septic shock and elevations are associated with increased death. BNP increases with initial sepsis severity and is associated with early left ventricular dysfunction that, in itself, is associated with later death. Monitoring BNP in early sepsis to identify occult left ventricular dysfunction may prompt earlier use of inotropes, which are not commonly used in early sepsis resuscitation.

For patients with suspected or known cardiac dysfunction, the addition of inotropic therapy is recommended. Dobutamine is the first-line agent for treatment of cardiac dysfunction in patients with sepsis. The management of patients with a cardiac component to their shock state presents a unique challenge to the clinician because they require the titration of vasopressors and inotropic agents. In this subset of patients, the use of a pulmonary artery catheter can be extremely useful. This allows for the specific titration of vasopressors based on systemic vascular resistance and inotropic agents based on cardiac output. There is no evidence to support increasing cardiac index to supranormal levels.

**Steroids in Septic Shock**

The use of steroids for the management of septic shock has been debated for several decades. In recent years, the concept of relative adrenal insufficiency in septic shock
has received renewed interest. Despite several large clinical trials addressing the issue of steroid use in patients with septic shock, the topic remains controversial. The ongoing debate is primarily on the definition of relative adrenal insufficiency in critically ill patients and the gold standard for diagnosing adrenal insufficiency in this population.

Previously, it was common practice to perform a low-dose ACTH (cosyntropin) stimulation test on all patients with septic shock as a means to identify those patients with relative adrenal insufficiency. To perform the cosyntropin stimulation test, a baseline serum cortisol is drawn which represents time zero (T0). The patient is then given 250 μg of IV cosyntropin. Subsequent serum cortisol levels are measured at 30 (T30) and 60 (T60) minutes after the cosyntropin. If the delta cortisol is less than or equal to 9 μg/dL then the patient is considered to have relative adrenal insufficiency and steroids are initiated. Based on the current evidence to date, it is now recognized that the ACTH stimulation test is not recommended to be used in this fashion among septic patients. Several factors interfere with the ACTH stimulation test, and current diagnostic tests are not accurate. Etomidate, which is commonly used for intubation causes a temporary suppression of the hypothalamic-pituitary-adrenal axis, resulting in transient adrenal insufficiency. In addition, patients that have received steroids at any time during the previous 6 months should not undergo testing of their adrenal function. Instead, these patients should be empirically initiated on steroid therapy. The current edition (2008) of the Surviving Sepsis Campaign Guidelines recommends that IV hydrocortisone should be considered for adult septic shock when hypotension responds poorly to adequate fluid resuscitation and vasopressors. The literature indicates that low-dose corticosteroids decrease the time to cessation of vasopressors, increase the systemic vascular resistance and MAP, and decrease the risk of death. The dose of hydrocortisone should be less than or equal to 300 mg/d. The author currently gives hydrocortisone 50 mg IV every 6 hours. The duration of steroid administration also remains controversial. The current recommendation is that steroids be discontinued once vasopressors are no longer required.

**Identifying the Source of Infection**

Identifying the source of infection is essential to sepsis management. Whenever possible, cultures should be obtained before initiation of empiric antimicrobial therapy. Current recommendations include obtaining a minimum of two blood cultures, including one blood culture from each vascular access device and one blood culture from a peripheral puncture. Additional cultures from other sites (eg, respiratory, urinary tract) and radiographic imaging are dictated by clinical suspicion. In the surgical population this may include obtaining cultures from surgical drains and performing pertinent imaging to identify an undrained abscess. Despite the importance of source identification, difficulty in the collection of cultures should not generate a significant delay in the administration of antimicrobial therapy.

To improve the chances of detecting bacteremia it is crucial to obtain the appropriate volume of blood for the culture medium. Several studies demonstrate that the volume of blood cultured is the single-most important factor in the detection of bacteremia. The recommend volume of blood per culture tube is greater than or equal to 10 mL. Obtaining blood cultures from all vascular access devices along with simultaneous collection of blood cultures from a peripheral site is beneficial in diagnosing catheter-related infections. The concept of differential time to positivity is well described. Differential time to positivity is defined as the difference in time necessary for blood cultures drawn simultaneously from a peripheral site and a central venous catheter to become positive. The differential time to positivity is considered
to be positive if the blood culture that is drawn through the vascular access device becomes positive at least 120 minutes before the peripheral culture. If a patient has an indwelling vascular access device and the cultures drawn from that device become positive at least 120 minutes before the peripheral cultures become positive, it is recommended that the device be removed because it is likely infected.\textsuperscript{50}

**Initiation of Empiric Antimicrobial Therapy**

Another key component of the initial resuscitation of the septic patient is the administration of IV antimicrobial therapy. Antimicrobials should be administered after appropriate cultures are collected but within 1 hour of sepsis recognition. Difficulty with specimen collection should not delay the initiation of antibiotic therapy. The time to antimicrobial administration is a critical factor in survival of patients presenting with sepsis. A recent study by Kumar and colleagues\textsuperscript{13} found that each hour in delay of antimicrobials was associated with an average decrease in survival of 7.6%. Delayed administration of antifungal therapy in subjects with *Candida* bloodstream infections was an independent predictor of hospital mortality.\textsuperscript{52} Maintaining a supply of commonly used antimicrobials in the ED and ICU can assist in the timely administration of these agents. The Surviving Sepsis guidelines recommend initiation of IV broad-spectrum antibiotics within the first hour of recognizing severe sepsis and septic shock.

The selection of antimicrobial therapy should take into account the patient’s history of drug allergies, recent antimicrobial exposure, suspected source of infection, and hospital-specific antibiograms. Within the author’s surgical ICU, the multidisciplinary sepsis team has developed antimicrobial regimens based on suspected source of infection and the current institution specific antibiogram (see Table 1). When choosing empiric antimicrobial therapy, a few general rules should be applied. Chiefly, the initial antimicrobial coverage should be broad enough to cover all potential pathogens. Evidence suggests that administering inadequate initial antimicrobial coverage is associated with increased morbidity and mortality.\textsuperscript{53–56} Any antimicrobial that the patient has recently received should be avoided. Vigilant monitoring of culture data and de-escalation of the antimicrobial regimen based on culture results and sensitivities will reduce the risk of superinfection and the emergence of resistant organisms.

**Obtaining Source Control**

The final component of the resuscitation bundle is identification and source control of the infection. This can be as simple as removing an infected vascular access device. However, in the author’s experience, in surgical patients the abdomen is the site of infection in greater than or equal to 50% of cases. These patients often require diagnostic imaging to identify the source and an operative procedure to attain source control. This includes, but is not limited to, emergent debridement of necrotic tissues, abscess drainage, removal of infected vascular access devices, and exploratory laparotomy. In the setting of septic shock, these procedures, although necessary, can present a unique challenge to the surgical team.

The concept of damage control laparotomy (DCL) was first recognized for the care of critically injured trauma patients.\textsuperscript{57–59} Damage control is defined as rapid, initial control of hemorrhage and contamination followed by intraperitoneal packing, as needed, and temporary abdominal closure. This concept was used on patients presenting with severe physiologic derangements such as coagulopathy, acidosis, and hypothermia. Instead of persisting for hours performing the definitive operation, these patients have their critical surgical issues addressed in an abbreviated manner so they may be taken to the ICU for continued resuscitation. Once the physiologic
derangements are corrected, the patient is taken back to the operating room for a definitive surgical procedure. The decision to use DCL should not be viewed as a bailout. Instead, it is a deliberate decision to truncate the surgical procedure to complete resuscitation and restore organ function to as normal as possible. The decision to perform DCL is often made before arriving in the operating room and is based on the severity of the patient’s physiologic derangements at the time of presentation.

The concept of DCL has evolved to include critically ill patients with surgical sepsis. Like the trauma patient with the lethal triad of acidosis, hypothermia, and coagulopathy, many patients with septic shock present in a similar fashion. For those patients presenting with septic shock and an identified source of infection requiring surgical intervention, the use of DCL can be life saving. As patients progress from sepsis with SIRS through severe sepsis with organ dysfunction into septic shock, the abdominal infection often turns into an abdominal catastrophe. The surgeon needs to recognize that these patients are in the persistent septic shock cycle (see Fig. 3). This is characterized by excessive proinflammation, which causes vasodilation, hypotension, and myocardial depression. This, combined with endothelial activation and diffused intravascular coagulopathy, causes ongoing endothelial leak, cellular shock, and microvascular thrombosis. The clinical manifestation is septic shock with progressive multiple organ failure. The crucial question for the managing surgeon is timing of the operative intervention for source control to break this persistent cycle. These patients are hemodynamically unstable and are clearly not optimal candidates for operative interventions. The traditional approach is to take the patient to the operating room and perform a definitive operation (see Fig. 4). However, this often results in a patient who is underresuscitated, hypoperfused, and in septic shock being treated for prolonged periods in the operating room with vasopressors being used to maintain blood pressure. The end result is early deaths from fulminant multiple organ failure or acute kidney injury. However, with the recent EBGs recommending source control within 6 hours, a paradigm shift was proposed (see Fig. 4).

The first priority is to initiate resuscitation. The patient needs to undergo preoperative optimization, during which time the airway is secured, central venous and arterial lines are placed, volume resuscitation and broad-spectrum antimicrobial agents are administered, and, if needed, vasopressors are titrated to the appropriate endpoints. Within 6 hours, the patient is taken to the operating room for emergent laparotomy and potential damage control procedures. The surgeon needs to assess the degree of physiologic derangement early in the operation and, if severe physiologic derangements exist, the operative interventions need to be abbreviated. The primary aim is to control the source of infection. Ostomies are not formed. Bowel resections remove necrotic or perforated bowel, but the bowel is left in discontinuity. Abdominal closure is with a temporary abdominal closure device and the patient is returned to the ICU for physiologic optimization. This includes optimizing volume resuscitation and mechanical ventilation, correction of coagulopathy and hypothermia, and monitoring for ACS. Over the next 24 to 48 hours, abnormal physiology is corrected so that the patient can safely return to the operating room for a definitive operation and abdominal closure.

One of the problems with this damage control strategy is that the midline abdominal fascia cannot be closed at the second operation because of bowel distention and edema. These patients require multiple additional laparotomies for definitive abdominal wall closure. The midline fascia is progressively closed with the use of a vacuum-assisted closure (VAC) device. For this technique to work it is important that the bowel not become adherent to peritoneum of the anterior abdominal wall or to the lateral paracolic gutters because, otherwise, the abdomen becomes “frozen” and the fascia cannot be brought to midline. The VAC device actively removes fluid and decreases
Table 1  
Antibiotic agent selection for empiric treatment based on suspected site of infection

<table>
<thead>
<tr>
<th>Indication</th>
<th>Antibiotic Drug</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>If vancomycin allergy (not intolerance), then</td>
<td>use linezolid</td>
<td>600 mg IV q 12 h</td>
</tr>
<tr>
<td>Indication</td>
<td>1. Preferred therapy</td>
<td>—</td>
</tr>
<tr>
<td>2. Severe β-lactam allergy</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Community-acquired pneumonia (CAP)</td>
<td>1. Ceftriaxone + levofloxacin</td>
<td>1 g IV q 24 h</td>
</tr>
<tr>
<td></td>
<td>2. Aztreonam + levofloxacin</td>
<td>a750 mg IV q 24 h</td>
</tr>
<tr>
<td>Aspiration (not chemical pneumonitis)</td>
<td>Piperacillin or tazobactam</td>
<td>a4.5 g IV q 6 h</td>
</tr>
<tr>
<td>Ventilator-associated pneumonia (VAP)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Early (&lt;5 d)</td>
<td>1. Cefepime</td>
<td>a2 g IV q 12 h</td>
</tr>
<tr>
<td></td>
<td>2. Ciprofloxacin</td>
<td>a400 mg IV q 12 h</td>
</tr>
<tr>
<td>Late (≥5 d)</td>
<td>1. Cefepime + vancomycin +</td>
<td>a2 g IV q 8 h</td>
</tr>
<tr>
<td>Pseudomonas risk: previous hospital or broad-</td>
<td>tobramycin</td>
<td>a15 mg/kg IV q 12 h</td>
</tr>
<tr>
<td>spectrum antibiotic exposure + pseudomonas</td>
<td>2. Ciprofloxacin + vancomycin +</td>
<td>a400 mg IV q 8 h</td>
</tr>
<tr>
<td>culture</td>
<td>tobramycin</td>
<td>a15 mg/kg IV q 12 h</td>
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<tr>
<td>Catheter-related</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Urinary catheter; UTI</td>
<td>1. Cefepime</td>
<td>a1 gm IV q 12 h</td>
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<tr>
<td></td>
<td>2. Ciprofloxacin</td>
<td>a400 mg IV q 12 h</td>
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<tr>
<td>IV, Art cath; bloodstream</td>
<td>Vancomycin</td>
<td>a1 gm IV q 12 h</td>
</tr>
<tr>
<td>Candidemia high-risk (TPN, steroid Tx, diabetes,</td>
<td>Fluconazole</td>
<td>a800 mg IV q 24 h</td>
</tr>
<tr>
<td>hepatic failure)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Wound/Soft tissue</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Necrotizing fasciitis</td>
<td>1. Piperacillin or tazobactam +</td>
<td>a4.5 g IV q 6 h</td>
</tr>
<tr>
<td></td>
<td>vancomycin + clindamycin</td>
<td>a15 mg/kg IV q 12 h</td>
</tr>
<tr>
<td></td>
<td>2. Ciprofloxacin + vancomycin +</td>
<td>a400 mg IV q 8 h</td>
</tr>
<tr>
<td></td>
<td>tobramycin + clindamycin</td>
<td>a15 mg/kg IV q 12 h</td>
</tr>
<tr>
<td>Surgical site</td>
<td>1. Ertapenem + vancomycin</td>
<td>a1 gm IV q 24 h</td>
</tr>
<tr>
<td></td>
<td>2. Ciprofloxacin + vancomycin</td>
<td>a400 mg IV q 12 h</td>
</tr>
<tr>
<td>Intra-abdominal</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Pseudomonas low-risk</td>
<td>1. Ertapenem + vancomycin</td>
<td>a1 gm IV q 24 h</td>
</tr>
<tr>
<td></td>
<td>2. Ciprofloxacin + metronidazole</td>
<td>a400 mg IV q 8 h</td>
</tr>
</tbody>
</table>

(continued on next page)
edema, provides medial tension, which helps to minimize fascial retraction and loss of domain, and protects the abdominal contents by providing separation between abdominal wall and viscera, with no fascial damage because it does not require fascial suture placement. Traditionally, abdominal wall defects in these frozen abdomens were closed by mobilizing skin or subcutaneous tissue flaps to cover the defect (ie, accepting a large hernia defect and need for delayed reconstruction) or by bridging the defect with mesh with later split thickness skin grafting once granulation tissue has developed. This is associated with a 20% gastrointestinal fistula rate, which is an extremely morbid complication. Additionally, many of these patients required delayed complex abdominal wall reconstructions. Recently, there has been significant enthusiasm for acute reconstruction with biologic mesh. Unfortunately, long-term follow-up studies show that many of these patients still require delayed hernia repairs of large defects. In the author’s published experience of treating the open abdomen with the VAC device, primary fascia closure was achieved in 87% of cases at a mean 7 days with a 2% fistula rate and no intraabdominal abscesses. These results are nearly identical to the results reported by Miller and colleagues from Wake Forest University.

Table 1 (continued)

<table>
<thead>
<tr>
<th>Antibiotic Drug Regimen</th>
<th>If vancomycin allergy (not intolerance), then use linezolid</th>
<th>600 mg IV q 12 h</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pseudomonas high-risk</strong></td>
<td>1. Imipenem or cilastatin + vancomycin</td>
<td>500 mg IV q 6 h</td>
</tr>
<tr>
<td><strong>Previous hospitalization or broad-spectrum antibiotic culture; + pseudomonas</strong></td>
<td>2. Ciprofloxacin + metronidazole + vancomycin</td>
<td>400 mg IV q 8 h</td>
</tr>
<tr>
<td><strong>Candidiasis high risk</strong> (TPN, steroid Tx, diabetes, hepatic failure, upper GI perf + H2 blocker, age ≥75, prolonged antibiotic, long-term care)</td>
<td>Consider fluconazole</td>
<td>800 mg IV q 24 h</td>
</tr>
</tbody>
</table>

**Abbreviations:** Art cath, arterial catheter; Dysfxn, dysfunction; GI perf, gastrointestinal perforation; H2, histamine type 2; TPN, total parenteral nutrition; Tx, therapy; UTI, urinary tract infection.

a Monitor; adjust if renal dysfunction.

b Kinetic monitoring.

![Fig. 3. The persistent septic shock cycle. DIC, diffused intravascular coagulopathy; MOF, multiple organ failure.](image-url)
More recently, Cothren and colleagues\textsuperscript{64} have reported 100% primary fascial closure rate using a modified VAC device technique. The long-term outcomes are not known; however, in short-term follow-up (mean 180 days) ventral hernia was 2.3%. However, as is true with all emergency laparotomies, this rate will increase with time.

In addition to damage control scenarios, there are other reasons to leave the abdomen open and plan for a staged relaparotomy. Patients with ischemic bowel that have undergone a resection will be taken back the next day to assess viability of the remaining bowel before attempts at anastomosis or ostomy creation. The author has been successful in completing the small bowel to colon anastomosis at the second operation and, thus, these patients have avoided the need for a temporary ileostomy. For patients with necrotizing pancreatitis, the attempt is to avoid an operative intervention but, occasionally, it becomes necessary. Patients who have massive bowel distention that cannot be closed without causing significant intraabdominal hypertension will undergo temporary abdominal closure. Intraabdominal hypertension sets the stage of ACS, which occurs with subsequent ICU resuscitation.\textsuperscript{65} Avoiding ACS significantly improves survival. Patients who develop ACS require a decompressive laparotomy. ACS is increasingly being recognized in nontrauma ICU patients, including those experiencing sepsis.\textsuperscript{66–68}

The author’s SICU has been using DCL for our patients with septic shock. Over 2 years, 22 patients underwent DCL for source control. Sources of intraabdominal infection were colon (11 patients), small bowel (4), stomach (2), and pancreas (1). Four patients had peritonitis with no identified source. Of the 22 patients, 6 died from multiple organ failure, for an actual mortality rate of 27%. The mean P-POSSUM (portsmouth predictor modification of the physiological and operative severity score for the enumeration of mortality and morbidity) predicted mortality was significantly higher at 69.4% (\(P<.02\)), as was the predicted mortality of 76% based on a mean APACHE (acute physiology and chronic health evaluation) II score of 31.8 (\(P<.02\)).\textsuperscript{69} These data suggest that the implementation of DCL for patients with surgical sepsis is decreasing mortality and is a viable option for patients with septic shock and the need for immediate operative source control.

**COMPUTERIZED CLINICAL DECISION SUPPORT TO HELP IMPLEMENT EBGS**

In an attempt to improve sepsis-related outcomes, EBGs were developed for the management of sepsis.\textsuperscript{12} When bedside clinicians are able to effectively implement
these EBGs, patient outcomes improve significantly. However, an alarmingly low percentage of patients with sepsis actually receive timely, evidence-based care. The relationship between compliance with evidence-based guidelines for sepsis and mortality has been well established. A study by Gao and colleagues demonstrated a twofold increase in hospital mortality in patients who did not receive the 6-hour sepsis bundle. In addition, noncompliance with the 24-hour sepsis bundle was associated with a 76% increase in risk for death. A recent multicenter, prospective study of over 15,000 subjects documented that only one-third of all subjects with sepsis receive appropriate evidence-based care. This inability to consistently implement EBGs represents a significant gap between the best available evidence and the ability to effectively implement that knowledge at the patient’s bedside. This gap can be bridged by leveraging technology in the form of computerized clinical decision support (CCDS) to aid bedside clinicians in consistently implementing EBGs at the bedside. Compliance with EBGs for the management of sepsis improves survival. However, achieving high levels of compliance remains extremely challenging. This is due to the complexity of the EBGs. The use of a CCDS program improves compliance with EBGs in multiple clinical settings, including the management of adult respiratory distress syndrome, management of intracranial pressure, and hemorrhagic shock resuscitation. This investigative team has developed a CCDS program for the early identification of sepsis. The implementation of a CCDS program for the management of sepsis will dramatically improve compliance with the EBGs, thereby improving patient outcomes.

**SUMMARY**

Sepsis in the surgical patient continues to be a common and potentially lethal problem. Early identification of patients and timely implementation of evidence-based therapies continue to represent significant clinical challenges for care providers. The implementation of a sepsis screening program in conjunction with protocol for the delivery of evidence-based care and rapid source control can improve patient outcomes.

**REFERENCES**


