Chapter 12
Source Control in Sepsis

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Introduction

Source control is generally accepted to be a key component in the treatment and reversal of sepsis. It is comprised of the physical efforts to remove or contain a focus of invasive infection in order to restore normal function [1]. The principles of source control for sepsis have been known for centuries, but only recently have prioritizing and achieving source control in sepsis become more recognized due to the heightened awareness of sepsis as a result of the Surviving Sepsis Campaign [2]. The majority of research in sepsis has focused on early diagnosis, resuscitation, antibiotics, and other therapies, and despite source control being the cornerstone of therapy for sepsis for centuries, it has not been widely studied. Due to this lack of evidence, source control is often overlooked or underutilized much to the detriment of septic patients.

Definition

Source control is generally defined as an intervention designed to eradicate or limit a focus of infection and is achieved in one of three ways: drainage, debridement, or definitive control via resection or device removal [3]. Traditionally source control was achieved through surgical intervention, but due to technological advancements, source control is increasingly achieved via less invasive measures such as radiological-directed percutaneous drainage. Regardless of the method, source

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control must provide a prompt, effective means to allow egress of infection from the infected site or complete removal of the offending source (necrotic organ, dead tissue, or infected foreign body).

Diagnosis

Patients with evidence of infection should be thoroughly evaluated for the source of infection. The Surviving Sepsis Campaign urges routine screening of potentially infected seriously ill patients for severe sepsis in order to provide earlier therapeutic interventions [2]. Despite increases in technology, the key to detecting patients with severe infections remains a thorough history and physical exam. A majority of infections requiring source control can be identified early on with this simple evaluation alone. Laboratory testing should then be undertaken to narrow the differential diagnosis and alert the clinician to significant physiologic derangements requiring intervention. Finally, multiple radiographic modalities are available to aid in diagnosis with the choice of study determined by the clinical suspicion of the treating provider. Although modern radiographic techniques deliver exceptional quality images and frequently identify the source of infection, there are some disease processes in which obvious emergent source control should be undertaken and radiographic imaging omitted to avoid delays to definitive therapy. The best example of this is the patient with florid peritonitis who needs no further diagnostic imaging and should be taken to the operating room for exploration. In this setting, further diagnostic workup only delays source control and sets the stage for worsened outcomes.

Drainage

Drainage is the evacuation of infected fluid from a closed abscess space. Drainage may be achieved via a surgical incision, or for infections not requiring operative intervention, with placement of a percutaneous catheter. The goal of drainage procedures is to convert an uncontrolled, closed-space infection under pressure into a controlled sinus or fistula that freely drains the infection. Frequently, the systemic manifestations of sepsis are abrogated by draining the infection, and this serves as the physiological basis of the clinical axiom that "pus under pressure" kills patients.

Superficial abscesses that can be easily accessed should be opened surgically; however, deeper space infections frequently require an intervention using radiographic guidance. Using ultrasound or CT guidance, a catheter can be inserted into the abscess to achieve decompression and drainage of the abscess. Percutaneous drainage using radiographic imaging has been demonstrated to be a safe and effective method of controlling sepsis in both intra-abdominal and thoracic abscesses [4, 5]. Percutaneous drainage techniques are most effective when the abscess is uniloculated.

Cinat et al. demonstrated that a successful outcome following percutaneous drainage is most likely when abscesses are postoperative, not pancreatic, and not infected with yeast [6].

Despite significant advances in radiographic techniques and percutaneous catheters, deep-space infections, particularly those with a large burden of necrotic tissue, cannot always be treated with percutaneous drainage. In patients with multiloculated abscesses, in patients with anatomically inaccessible abscesses, or in patients who have failed percutaneous drainage, open drainage is often required to achieve adequate drainage. The failure to recognize unsuccessful drainage or delays in operative drainage frequently lead to worsened outcomes in septic patients. It should be noted that a partially effective drainage procedure may be an effective temporizing maneuver that allows correction of severe physiologic derangements such that definitive, operative intervention may be performed in a more stable patient.

Debridement/Device Removal

Infected or necrotic tissue incites a vigorous inflammatory response in patients and should be excised when possible. Necrotizing soft tissue infections can spread rapidly and require early and extensive debridement to control the infection. Other necrotizing processes without infection, such as necrotizing pancreatitis, may be debrided after demarcation of the necrotizing tissue provided that the patient is stable enough to undergo surgical exploration. In fact, delayed debridement of necrotizing pancreatitis may lead to improved outcomes, but this remains controversial [7, 8].

Medical devices are frequently the source of infection in septic patients. Infections of these foreign bodies are difficult to eradicate due to the bacteria's ability to generate a biofilm that promotes adherence to the foreign body and prevents effective penetration of host defenses and antibiotics. Due to these factors, device removal is recommended whenever possible. Attempts to "eradicate" infection from an infected foreign body are rarely successful, and the infection typically flares as soon as the suppressive effect of antibiotics is removed.

Definitive Control

The ultimate source control frequently requires operative intervention to remove the focus of infection and repair the affected organ. This category includes resection for appendicitis or cholecystitis, repair of intestinal perforations, and resection of nonviable bowel or organs. Although these interventions frequently require the most invasive procedure, the operations result in the most definitive source control and frequently eliminate the need for any further interventions. For example, cholecystectomy for gangrenous cholecystitis completely removes the source of sepsis, unlike decompression with a cholecystostomy tube which only drains the infection, leaving the infected wall of the gallbladder to drive the host's septic response and may ultimately require future cholecystectomy for definitive restoration of normal function.

Indications for Source Control

Early goal-directed therapy increases survival in patients with severe sepsis or septic shock, but fluid resuscitation and antibiotics may not be sufficient therapy for patients with infections requiring source control [9]. As outlined in the Surviving Sepsis Guidelines [2], a specific anatomical diagnosis of infection should be sought as quickly as possible. In many cases, the identification of the infectious source of sepsis is frequently delayed or overlooked as the clinician focuses on the resuscitation of the critically ill patient. In fact, patients may be admitted to the intensive care unit with a diagnosis of sepsis, without a differential diagnosis of the source of sepsis and often without a clear-cut diagnosis other than "sepsis." All patients with severe sepsis or septic shock should have an attempt at identifying the source of infection because emergent source control is as important, if not more important, as the early recognition of sepsis and resuscitation in patients.

When source control is deemed necessary, interventions aimed to obtain it should be made as soon as possible. Invariably some procedures can be delayed for a limited period of time as the necessary institutional resources are mobilized and personnel become available, but it is imperative that patients are closely monitored during these inevitable delays. Additional therapies such as fluid and blood administration and antibiotics should be given during this period of preparation. Thus, the timing of source control depends on the severity of the patient's illness and can be broadly divided into emergent or urgent interventions.

Emergent source control is required in patients with severe, life-threatening infections or in those patients with poor premorbid physiological reserve who will not tolerate the sequelae of the septic response. These patients typically present with extensive physiologic derangements and organ failure. Patients in this group should be quickly identified, and immediate resuscitation and antibiotic therapy should be initiated. Source control should then be obtained, even if the patient has not been fully resuscitated, as the resuscitation can be continued in the operating room or interventional radiology suite. Although surgeons have classically performed emergent source control as part of their standard care of septic patients, there is a paucity of data on the effect of timing on patient outcomes. Nonetheless, some examples of infections requiring immediate source control include diffuse peritonitis, necrotizing soft tissue infections, and infections causing hemodynamic instability [10–12]. In patients requiring emergent source control, time is critical, and delays in obtaining source control in this patient group are associated with worsened outcomes [13].

For those patients whose physiological derangements are less severe or in those patients who have greater physiological reserve and less medical comorbidities, delayed source control may be desirable. In these patients, the risk of emergent intervention may be unnecessarily high and may be lessened by a brief period to allow adequate fluid resuscitation, correction of electrolyte abnormalities, reversal of coagulopathy, etc. A short delay in order to maximize surgical and anesthesiologist technical ability, operating room preparedness, and other resources may also be acceptable. Finally, image-guided drainage of an abscess is frequently the initial intervention of choice, but this may necessitate a delay until the interventional radiology team is available. While the concept of an “acceptable delay” seems counter to the expressed concept of emergent source control, this delay should only be undertaken if the cost in terms of time delay will be offset with a significant reduction in risk to the patient, or added benefit. In essence, a brief delay that favorably alters the risk to benefit ratio to the patient is worth undertaking, but any delay that does not yield reduced risk or added benefit must be avoided.

The appropriate delay to source control in non-emergent cases remains controversial because there is limited evidence. One consensus of experts accepts a delay of up to 24 h for patients with intra-abdominal sepsis in hemodynamically stable patients without peritonitis [14]. Appendicitis is the best-studied disease process looking at delays in source control. Although there is still some debate over delaying appendectomy, it appears that for most patients an in-hospital delay of less than 24 h is acceptable [15, 16]. However, in all cases of delayed source control, patients must be carefully monitored to ensure no deterioration in their clinical status. If they do worsen, immediate source control should be undertaken. Additionally, if there are no barriers to early source control, intervention should be undertaken as soon as possible to minimize complications.

Method of Source Control

The method used to obtain source control will vary depending on multiple factors, but ideally the method that results in adequate source control through the least invasive means is generally the most desirable. The clinician must weigh the risks and benefits of less or more invasive methods of source control to determine the appropriate modality. Integral to this decision process is an understanding of the natural history of each proposed therapy, as well as an understanding of limitations, common pitfalls, and complications since all of these factors must be considered in the decision analysis process. Often, the most invasive intervention must be performed in order to achieve rapid, effective source control.

Traditionally source control required surgical intervention to drain or remove the source of infection. The advent of advanced radiographic imaging and access techniques has allowed many infections to be controlled with less invasive procedures. Gerzoff et al. demonstrated that percutaneous drainage of intra-abdominal abscesses could be done safely and effectively using radiographic guidance [4]. The use of percutaneous drainage of both intra-abdominal and intra-thoracic infections is now commonplace [5, 17]. Successful percutaneous drainage of deep space infections controls the source of sepsis and delays or even eliminates the need for surgical intervention. Generally, percutaneous drainage procedures minimize the anatomic and physiologic derangements compared with surgical intervention, but the efficacy of drainage may be less definitive than surgical methods.

Despite significant advances in imaging and drainage techniques, treatment failures with percutaneous drainage still occur. Success rates for percutaneous drainage range from 70 to 90% depending on the source (location) of the infection [4, 6, 18, 19]. Multiple factors have been identified that predict failure of percutaneous drainage, including size of the abscess, poorly defined abscess, abscess that is not postoperative, abscess with yeast infection, residual collection after first drainage attempt, and increased number of drainage attempts [4, 17–19]. Patients being managed with percutaneous source control require frequent reassessment of the adequacy of source control, and if the patient clinically deteriorates, then more aggressive, and typically more invasive, source control is warranted.

Operative intervention is often required to obtain the best source control. Surgery facilitates drainage of abscesses and has the added benefit of removal of the offending source of the infection. Surgical therapy may employ resection (appendix, gallbladder, ischemic bowel, necrotizing soft tissue infection) or repair (duodenal ulcer, intestinal perforation). This intervention frequently controls the source of sepsis more completely, which may ultimately shorten the duration of physiological derangement and generally decreases the need for future interventions. It is notable though that once multisystem organ failure has occurred, surgical source control of the infection may not result in reversal of organ failure [20, 21].

Severe intra-abdominal infections resulting in sepsis are frequently complicated by postoperative abdominal compartment syndrome (ACS). ACS is defined as intra-abdominal hypertension resulting in multisystem organ failure driven by the accumulation of fluid within the abdomen and its contents restricted by the noncompliant abdominal fascia. The fluid may be tissue fluid or blood that exceeds the capacitance of the abdominal cavity leading to increased pressure. A planned open-abdomen approach, in which the abdomen is closed with a temporary abdominal dressing, is an accepted method of preventing ACS. Recurrent ACS may occur even in the setting of an open abdomen and portends a dismal prognosis. The open abdomen may facilitate repeat laparotomy and washout of intra-abdominal sepsis; however, there has been no convincing data that planned re-laparotomy improves outcomes in these patients [22]. The benefits of an open abdomen must be balanced against the complications since these patients have higher rates of anastomotic leak, entero-cutaneous fistula, and massive hernia [22–24]. Therefore, a planned open abdomen should be reserved for cases requiring a second look (bowel ischemia), to restore intestinal continuity after an abbreviated laparotomy in a critically ill patient or in patients with abdominal compartment syndrome. At present time there is insufficient data to recommend that the abdomen be left open in order to enhance source control [25].

Treatment of Selected Diseases

Gastrointestinal Tract

The gastrointestinal tract frequently is a source of severe sepsis and septic shock, with appendicitis ranking as the most common source of infection [26]. Although a short delay in appendectomy appears reasonable, patients with appendicitis should undergo appendectomy as soon as feasible in order to eliminate the infectious source. Like many surgical infectious diseases, the severity of the infection is on a continuum from mild physiological derangements extending all the way up to florid septic shock and multisystem organ failure. Accordingly, the optimal timing of intervention also spans a continuum, but it is critical that surgical source control not be deferred in patients manifesting clinical deterioration. In contrast to appendicitis, patients with intestinal perforations generally require emergent operative intervention to control the source of sepsis. The site of perforation will determine the extent of surgery required. The goals of therapy in these patients are to physically clear the infection as well as restore normal function if possible.

Sepsis from small and large bowel perforations requires an operation to control the perforation. Traditionally, control was obtained via resection of the diseased intestine, and in cases of severe sepsis and septic shock, bowel resection with a diverting ostomy remains the preferred method of source control. If the patient's physiology and comorbidities allow, lesser operations may suffice in obtaining some degree of source control without the additional burden of more invasive or definitive surgery. For example, in diverticulitis, an option may be laparoscopic drainage and lavage of the infection with definitive resection and anastomosis delayed until the sepsis and inflammation have resolved. A procedure such as this allows creation of a controlled fistula and avoidance of a colostomy while still draining the abscess in most patients [27].

Intestinal ischemia resulting in bowel compromise is a feared source of intra-abdominal sepsis. In some cases of intestinal ischemia, patients can be treated non-operatively with resuscitation and correction of the underlying cause of the ischemia; however intestinal infarction requires emergent operation to resect the segment of bowel affected. The diagnosis of intestinal ischemia can be challenging as physical exam, laboratory testing, and radiography can lack sensitivity; therefore, if suspected in a critically ill patient, operative exploration should be performed. Patients undergoing resection of necrotic bowel due to vascular catastrophe are best managed with a planned open abdomen and "second look" laparotomy to assure viable bowel prior to restoring bowel continuity [28].

Biliary Tract

The biliary tract is another frequent source of intra-abdominal sepsis, and the spectrum of illnesses ranges from simple non-complicated cholecystitis all the way up to ascending cholangitis and septic shock. Acute cholangitis is caused by biliary obstruction and systemic spread of the bacterial infection from the biliary tree into the liver and beyond. Obstruction of the biliary tree results in an increase in intraductal pressure leading quickly to translocation of bacteria into the bloodstream, resulting in severe sepsis and shock, with a high rate of mortality if not treated promptly. Acute cholangitis is often diagnosed based on the presence of three classic findings: right upper quadrant abdominal pain, fever, and jaundice. The mortality rate for this disease entity has traditionally been very high; prior to 1980, the mortality rate was 50 %, but this rate has dropped significantly in recent years with the rise of endoscopic decompression [29].

Treatment of acute cholangitis requires early diagnosis, prompt antibiotic therapy, and decompression of the biliary tree for source control. In severe cholangitis, antibiotics alone are insufficient, and emergent decompression must be performed. Decompression of the biliary tree can be accomplished via endoscopic, percutaneous, or surgical methods. The use of endoscopic retrograde cholangiopancreatography (ERCP) is effective in controlling sepsis and has been shown to have a lower morbidity and mortality than surgical approaches [30]. Delays in performing ERCP for cholangitis result in increased mortality, length of hospital stay, and readmission rates [31, 32].

Acute cholecystitis is a more common source of biliary sepsis, but usually causes less severe sepsis and shock than cholangitis. Laparoscopic cholecystectomy is the preferred method of source control when possible; however, in patients that are poor operative risk candidates, percutaneous drainage with a cholecystostomy tube is adequate to control the infection. A notable exception may be the previously noted condition of emphysematous cholecystitis in which bacterial invasion of the gallbladder wall by gas-forming organisms results in a gangrenous cholecystitis. In this setting, drainage procedures alone may be inadequate in controlling the source of infection, and extirpation of the infected organ may be necessary.

Pancreatitis

Pancreatitis, like many surgical infections, spans a range from chemical pancreatitis marked by mild elevations of laboratory tests to severe necrotizing pancreatic infections leading to death. Pancreatitis follows a variable and unpredictable course both in timing of disease progression and disease severity, making this a particularly dangerous and difficult disease to treat for clinicians. Patients with pancreatic infarction or necrosis are at risk of developing infected necrosis; however, the diagnosis is difficult to make on clinical grounds alone because the findings of fever, leukocytosis, and worsening organ failure are nonspecific and frequently occur in patients with severe pancreatitis with and without infection. Abdominal computed tomography is helpful in identifying pancreatic necrosis as well as the stigmata of infected pancreatic necrosis and is particularly helpful in guiding therapy. When infected pancreatic necrosis is identified, prompt drainage of the infection is required.

The timing and method of this drainage has been contested, but delayed surgical debridement appears to decrease the morbidity and mortality of pancreatic necrosectomy [7, 33, 34]. Therefore, initial control of infected pancreatic necrosis with percutaneous drainage should be considered in most patients with open necrosectomy reserved for only the sickest patients or those developing ACS. Percutaneous pancreatic drainage controls the liquid component of the infection and is a temporizing maneuver, but true source control requires surgical debridement of the solid, necrotic debris. Utilizing this "step-up" approach, true source control may be obtained in a way that has been shown to significantly reduce the mortality associated with operation for infected pancreatic necrosis [8].

Necrotizing Soft Tissue Infection

Necrotizing soft tissue infections have a mortality rate of 25–35% and an even higher rate of significant morbidity [35]. One of the most feared types of necrotizing soft tissue infections is necrotizing fasciitis. This rapidly progressive form of soft tissue infection can spread in a matter of hours, resulting in death of the patient. Source control via surgical debridement must be performed emergently if there is any hope of patient salvage, and the most important factor in preventing morbidity and mortality is time to surgical debridement. Indeed, multiple series have demonstrated that the only factor predictive of survival in the setting of necrotizing soft tissue infection is time to operative intervention [36, 37]. Patients with necrotizing soft tissue infections should be taken emergently to the operating room for wide excision and debridement. The extent of excision should extend beyond the obviously affected areas and frequently results in large open wounds. Although these wounds may result in significant morbidity, the risk of mortality increases substantially when debridement is incomplete [37]. After the initial debridement, wounds should be inspected within hours to ensure control of the infection, as many patients require serial debridement. In extreme cases, amputation of an extremity may be necessary because of rapidly spreading infection or worsening muscle necrosis due to bacterial invasion.

Infected Devices

The use of invasive medical devices is commonplace. Medical devices can range from simple devices used almost daily in the intensive care unit (urinary catheters, central venous catheters) to complex, life-saving devices (valve replacements, left ventricular assist devices). Unfortunately, medical devices frequently provide the nidus for infection in septic patients. Microbes are able to bind to these medical devices based upon the cell surface characteristics of the microorganisms and the type of foreign body material [38]. Once the device is colonized, the organisms produce a biofilm that protects the organisms from antibiotic therapy and results in persistent or difficult to eradicate infections [39].

The optimal treatment of an infected medical device is removal. Any patient with severe sepsis or septic shock related to a medical device should have prompt removal of the device and antibiotic therapy. Similarly to other infections, the urgency of removal depends on the clinical condition of the patient, but should be performed soon after identifying the device as the source.

Patients with implanted medical devices often have other potential sites for infection, making definitive diagnosis challenging. However, when possible or if a high degree of suspicion exists, the device should be removed. Additionally, the device should be removed if there is local skin infection, metastatic infective complications, or recurrence of infection after cessation of antibiotics [38]. Removal of the device can carry significant morbidity, such as in a patient with difficult vascular access or infected mesh from a hernia repair. Salvage therapy with antibiotics can be performed in stable patients in an attempt to avoid removal of the device; however, the presence of the foreign body and biofilm makes salvage attempts unsuccessful. Contingency plans should be arranged in the meantime in case of treatment failure, and salvage should not be attempted in patients with severe sepsis or shock.

Conclusion

Source control is a critical element in managing patients with sepsis, yet it is often overlooked by clinicians as they focus on fluid resuscitation, timing and selection of antibiotics, etc. In certain disease processes, such as necrotizing fasciitis or ascending cholangitis, source control is the most important step; therefore, early consideration of the source and prompt intervention are imperative. The timing of source control should be determined by the severity of the patient's condition, the expected course for that disease process, and the overall condition of the patient. The optimal method of source control is determined by evaluating the risks and benefits of the invasiveness of the therapy versus the need for partial or complete eradication of the source. In general, the method that provides the most complete control with the least disruption of anatomy is preferred.

References

1. Marshall JC, al Naqbi A. Principles of source control in the management of sepsis. Crit Care Clin. 2009;25:753–68.
2. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41(2):580–637.
3. Jimenez MF, Marshall JC. Source control in the management of sepsis. Intensive Care Med. 2001;27:S49–62.

4. Gerzof SG, Robbins AH, Johnson WC, Birkett DH, Nabseth DC. Percutaneous catheter drainage of abdominal abscesses. A five-year experience. N Engl J Med. 1981;305:653–7.
5. Moulton JS, Benkert RE, Weisiger KH, Chambers JA. Treatment of complicated pleural fluid collections with image-guided drainage and intracavitary urokinase. Chest. 1995;108(5): 1252–9.
6. Cinat ME, Wilson SE, Din AM. Determinants for successful percutaneous image-guided drainage of intra-abdominal abscess. Arch Surg. 2002;137(7):845–9.
7. Fernandez-del Castillo C, Rattner DW, Makary MA, Mostafavi A, McGrath D, Warshaw AL. Debridement and closed packing for the treatment of necrotizing pancreatitis. Ann Surg. 1998;228(5):676–84.
8. van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al. A setp-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med. 2010;362:1491–502.
9. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345:1368–77.
10. Gajic O, Urrutia LE, Sewani H, Schroeder DR, Cullinane DC, Peters SG. Acute abdomen in the medical intensive care unit. Crit Care Med. 2002;30(6):1187–90.
11. Boyer A, Vargas F, Coste F, Saubusse E, Castaing Y, Gbikpi-Benissan G, et al. Influence of surgical treatment timing on mortality from necrotizing soft tissue infections requiring intensive care management. Intensive Care Med. 2009;35(5):847–53.
12. Buck DL, Vester-Andersen M, Moller MH. Surgical delay is a critical determinant of survival in perforated peptic ulcer. Br J Surg. 2013;100(8):1045–9.
13. Wacha H, Hau T, Dittmer R, Ohmann C, The Peritonitis Study Group. Risk factors associated with intraabdominal infections: a prospective multicenter study. Langenbecks Arch Surg. 1999;384:24–32.
14. Solomkin JS, Mazuski JE, Bradley JS, Rodvold KA, Goldstein EJC, Baron EJ, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the surgical infection society and the infectious diseases society of America. Clin Infect Dis. 2010;50:133–64.
15. The United Kingdom National Surgical Research Collaborative. Safety of short, in-hospital delays before surgery for acute appendicitis. Ann Surg. 2014;259:894–903.
16. Drake FT, Mottey NE, Farrokhi ET, Florence MG, Johnson MG, Mock C, et al. Time to appendectomy and risk of perforation in acute appendicitis. JAMA Surg. 2014;149(8):837–44.
17. Kumar RR, Kim JT, Haukoos JS, Macias LH, Dixon MR, Stamos MJ, et al. Factors affecting the successful management of intra-abdominal abscesses with antibiotics and the need for percutaneous drainage. Dis Colon Rectum. 2005;49:183–9.
18. Kassi F, Dohan A, Soyer P, Vicaut E, Boudiaf M, Valleur P, et al. Predictive factors for failure of percutaneous drainage of postoperative abscess after abdominal surgery. Am J Surg. 2014;207:915–21.
19. Marin D, Ho LM, Barnhard H, Neville AM, White RR, Paulson EK. Percutaneous abscess drainage in patients with perforated acute appendicitis: effectiveness, safety, and prediction of outcome. Am J Roentgenol. 2010;194:422–9.
20. Eiseman B, Beart R, Norton L. Multiple organ failure. Surg Gynecol Obstet. 1977;144(3): 323–6.
21. Norton LW. Does drainage of intraabdominal pus reverse multiple organ failure. Am J Surg. 1985;149(3):347–50.
22. Hau T, Ohmann C, Wolmerhauser A, Wacha H, Yang Q. Planned relaparotomy vs relaparotomy on demand in the treatment of intra-abdominal infections. Arch Surg. 1995;130:1193–7.
23. van Ruler O, Mahler CW, Boer KR, Reuland EA, Gooszen HG, Opmeer BC, et al. Comparison of on-demand vs planned relaparotomy strategy in patients with severe peritonitis. JAMA. 2007;298(8):865–72.
24. Adkins AL, Robbins J, Villalba M, Bendick P, Shanley CJ. Open abdomen management of intra-abdominal sepsis. Am Surg. 2004;70(2):137–40.

25. Lamme B, Boermeester MA, Reitsma JB, Mahler CW, Obertop H, Gouma DJ. Meta-analysis of relaparotomy for secondary peritonitis. Br J Surg. 2002;89:1516–24.
26. Sartelli M, Catena F, Ansaloni L, Coccolini F, Corbella D, Moore EE, et al. Complicated intra-abdominal infections worldwide: the definitive data of the CIAOW study. World J Emerg Surg. 2014;9:37.
27. Toorenvliet BR, Swank H, Schoones JW, Hamming JF, Bemelman WA. Laparoscopic peritoneal lavage for perforated colonic diverticulitis: a systematic review. Colorectal Dis. 2010; 12(9):862–7.
28. Park WM, Glovicki P, Cherry KJ, Hallet JW, Bower TC, Panneton JM, et al. Contemporary management of acute mesenteric ischemia: factors associated with survival. J Vasc Surg. 2002;35(3):445–52.
29. Jamal MM, Yamini D, Singson Z, Samarasena J, Hashemzadeh M, Vega KJ. Decreasing hospitalization and the in-hospital mortality related to cholangitis in the united states. J Clin Gastroenterol. 2001;45:e92–6.
30. Lai E, Mok F, Tan E, Lo C, Fan S, You K, et al. Endoscopic biliary drainage for severe acute cholangitis. N Engl J Med. 1992;326:1582–6.
31. Kashab MA, Tariq A, Tariq U, Kim K, Ponor L, Lennon A, et al. Delayed and unsuccessful endoscopic retrograde cholangiopancreatography are associated with worse outcomes in patients with acute cholangitis. Clin Gastroenterol Hepatol. 2012;10:1157–61.
32. Navaneethan U, Gutierrez NG, Jegadeesan R, Venkatesh P, Butt M, Sanaka MR, et al. Delay in performing ERCP and adverse events increase the 30-day readmission risk in patients with acute cholangitis. Gastrointest Endosc. 2013;78:81–90.
33. Mier J, Luque-de Leon E, Castillo A, Robledo F, Blanco R. Early versus late necrosectomy in severe necrotizing pancreatitis. Am J Surg. 1997;173:71–5.
34. Hartwig W, Maksan SM, Foitzik T, Schmidt J, Herfarth C, Klar E. Reduction in mortality with delayed surgical therapy of severe pancreatitis. J Gastrointest Surg. 2002;6(3):481–7.
35. Anaya DA, McMahon K, Nathens AB, Sullivan SR, Foy H, Bulger E. Predictors of mortality and limb loss in necrotizing soft tissue infections. Arch Surg. 2005;140:151–8.
36. McHenry CR, Piotrowski JJ, Petrinic D, Malangoni MA. Determinants of mortality for necrotizing soft-tissue infections. Ann Surg. 1995;221:558–63.
37. Bilton BD, Zibari GB, McMillan RW, Aultman DF, Dunn G, McDonald JC. Aggressive surgical management of necrotizing fasciitis serves to decrease mortality: a retrospective study. Am Surg. 1998;64:397–400.
38. von Eiff C, Jansen B, Kohnen W, Becker K. Infections associated with medical devices. Drugs. 2005;65(2):179–214.
39. Costerton JW, Stewart PS, Greenberg EP. Bacterial Biofilms: a common cause of persistent infections. Science. 1999;284:1318–22.