Common Complications in the Critically III Patient

Kathleen B. To, MD, Lena M. Napolitano, MD*

KEYWORDS

- Venous thromboembolism Ventilator-associated pneumonia
- Central line-associated bloodstream infection
 Urinary tract infection
- Surgical site infection

KEY POINTS

- Critically ill patients in intensive care units (ICUs) are subject to many complications associated with the advanced therapy required for treatment of their serious illnesses.
- Many of these complications are health care-associated infections and are related to indwelling devices, including ventilator-associated pneumonia, central line-associated bloodstream infection, and catheter-associated urinary tract infection.
- Surgical site infection is also a common complication amongst surgical ICU patients.
- Venous thromboembolism, including deep venous thrombosis and pulmonary embolus, is another common complication in critically ill patients.
- All efforts should be undertaken to prevent these complications in surgical critical care, and national efforts are under way for each of these complications.

COMMON COMPLICATIONS IN THE CRITICALLY ILL PATIENT

Critically ill patients in intensive care units (ICUs) are subject to many complications associated with the advanced therapy required to treat their serious illnesses. Many complications are health care-associated infections (HAIs) related to indwelling devices. These complications include ventilator-associated pneumonia (VAP), central line-associated bloodstream infection (CLABSI), and catheter-associated urinary tract infection (CA-UTI). Surgical site infection (SSI) is also a common complication amongst surgical ICU (SICU) patients. Another common complication is venous thromboembolism (VTE), including deep venous thrombosis (DVT) and pulmonary embolus (PE). National efforts to prevent each of these complications are under

Division of Acute Care Surgery [Trauma, Burns, Surgical Critical Care, Emergency Surgery], Department of Surgery, University of Michigan Health System, Ann Arbor, MI, USA * Corresponding author. Room 1C340A-UH, University Hospital, 1500 East Medical Center Drive, Ann Arbor, MI 48109-5033.

E-mail address: lenan@umich.edu

surgical.theclinics.com

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way. In this article, epidemiology, risk factors, diagnosis, treatment, and prevention of these complications in critically ill patients are discussed.

HAIS IN THE ICU

HAIs are a significant cause of morbidity and mortality in the United States, with 1.7 million reported in 2002, of which 417,946 (24.6%) were among adults and children in ICUs. The estimated deaths associated with HAIs in US hospitals were 98,987: of these, 35,967 were for pneumonia, 30,665 for bloodstream infections, 13,088 for urinary tract infections (UTIs), 8205 for SSIs, and 11,062 for infections of other sites.¹ National data regarding HAIs in US ICUs were initially reported by the Centers for Disease Control and Prevention (CDC) National Nosocomial Infections Surveillance (NNIS) system, and is currently reported by the National Healthcare Safety Network (NHSN). Similar to the NNIS system, NHSN facilities voluntarily report their HAI surveillance data for aggregation into a single national database, which provides national data regarding HAIs. The NHSN was established in 2005 to integrate and supersede 3 legacy surveillance systems at the CDC: the NNIS system, the Dialysis Surveillance Network, and the National Surveillance of Healthcare Workers. NHSN has both a patient safety and a healthcare personnel safety surveillance component. In the patient safety component, there is a device-associated module (Fig. 1). The deviceassociated module includes 4 separate options: CLABSI, VAP, CA-UTI, and dialysis incident (DI). DI is used only by chronic outpatient dialysis centers.

CLABSI Epidemiology

ICU patients are at increased risk for CLABSI because 48% of ICU patients have indwelling central venous catheters (CVCs), accounting for 15 million central line

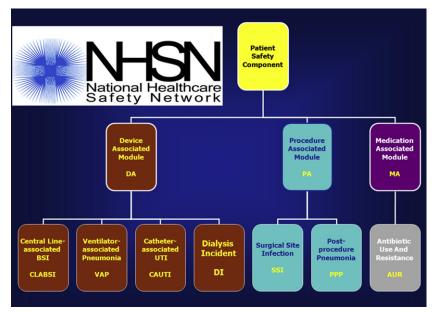


Fig. 1. The patient safety component of the NHSN of the CDC includes a device-associated module, including common HAIs in the ICU, including CLABSI, VAP, and CA-UTI.

days per year in US ICUs. CLABSIs are linked to mortality that ranges between 12% and 25% and result in increased ICU and hospital length of stay.

Risk Factors

The most significant risk factor for CLABSI is the presence of a CVC with duration of catheterization for more than 7 days.² Peripherally inserted CVCs (PICCs) are associated with a similar CLABSI rate compared with CVCs placed in the internal jugular or subclavian position.³ PICCs are associated with an increased risk for upper extremity DVT.⁴

Diagnosis

The new CDC definition for CLABSI was published in 2008 (**Box 1**).⁵ There are 3 potential routes of infection related to central lines: (1) extraluminal, from contiguous skin flora; (2) intraluminal, from contamination of the catheter hub and lumen or contamination of the infusate; and (3) hematogenous, from a distant unrelated site of infection (**Fig. 2**).

Treatment

Treatment principles for a CLABSI include removal of the infected device, and administration of empiric intravenous antimicrobials targeted against the likely causative bacterial pathogen and modified based on the final culture results. The Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection were updated in 2009. These guidelines review specific treatments based on pathogen identified, and whether complications (suppurative thrombophlebitis, endocarditis, osteomyelitis) are present (**Fig. 3**).⁶ Significant changes have occurred in the microbiology of CLABSI in US hospitals (**Fig. 4**). Coagulase-negative staphylococci remain the most common CLABSI pathogen, but there has been a significant increase in *Candida* as causative pathogens and a significant reduction in *Staphylococcus*

Box 1

Laboratory-confirmed bloodstream infection (LCBI)

LCBI criteria 1 and 2 may be used for patients of any age, including patients \leq 1 year of age.

LCBI must meet at least 1 of the following criteria:

1. Patient has a recognized pathogen cultured from 1 or more blood cultures

and

Organism cultured from blood is not related to an infection at another site.

2. Patient has at least 1 of the following signs or symptoms: fever (>38 $^\circ\text{C}$), chills, or hypotension

and

Signs and symptoms and positive laboratory results are not related to an infections at another site

and

Common skin contaminant (ie, diphtheroids [Corynebacterium spp], Bacillus [not B anthracis] spp, Propionibacterium spp, coagulase-negative staphylococci [including Staphylococcus epidermidis], viridians group streptococci [Aerococcus spp, Micrococcus spp]) cultured from 2 or more blood cultures drawn on separate occasions.

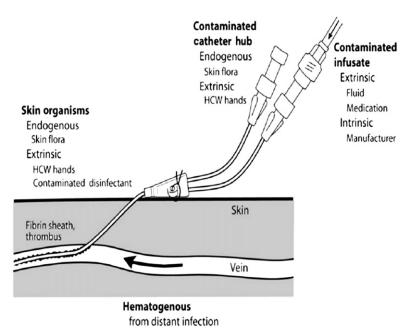


Fig. 2. Three potential routes of infection (CLABSI) related to central line use in critically ill patients.

aureus isolates (from 14.3% to 9.9% of all pathogens). Methicillin-resistant *S aureus* (MRSA) remains a common cause of CLABSI in US ICUs.

Prevention

Most CLABSI are preventable, and CLABSI prevention is important because the Center for Medicare and Medicaid Services (CMS) decided to disallow incremental payments associated with secondary conditions that it sees as preventable complications of medical care, including CLABSI, on October 1, 2008.⁷ The state of Michigan Keystone Project, beginning in 2003, significantly reduced the incidence of CLABSIs (66% reduction) in 108 Michigan ICUs within 18 months, using 5 evidence-based procedures: hand washing; full-barrier precautions during CVC insertion; chlorhexidine skin preparation; avoidance of femoral site placement; and removal of unnecessary CVCs as soon as possible. This project was credited with saving 1500 lives and \$200 million.⁸ The Keystone Project implemented the Comprehensive Unit-Based Safety Program (CUSP), which has expanded to hospitals nationwide and to other settings beyond ICUs ("On the CUSP: Stop BSI"). This effort was funded in large part by the Agency for Healthcare Research and Quality as part of an action plan to reduce the incidence of HAIs.⁹ A recent report by the CDC found that hospital ICUs decreased the number of CLABSI cases by more than half (58% reduction), from 43,000 in 2001 to 18,000 in 2009.¹⁰ This decrease represents up to 6000 lives saved and \$1.8 billion in cumulative excess health care costs saved since 2001.

What should we do to prevent CLABSIs? The Guidelines for Prevention of Intravascular Catheter-Related Infections^{11,12} were recently updated in 2011, replacing the previous 2002 guidelines. Major areas of emphasis include (1) educating and training health care personnel who insert and maintain catheters; (2) using maximal sterile

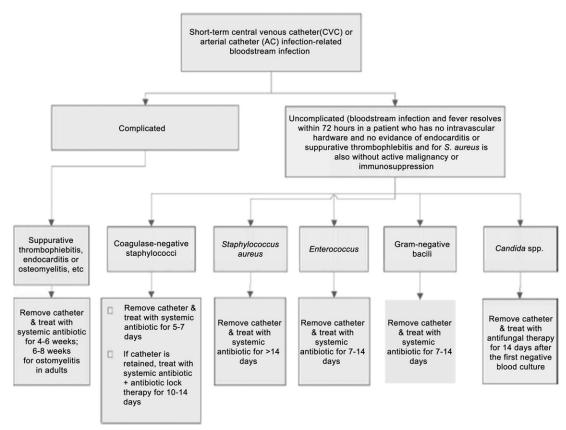


Fig. 3. Short-term CLABSI treatment includes removal of the CVC, adjustment of antimicrobial therapy based on the culture results, and variable duration of antimicrobial therapy based on the pathogen isolated and the clinical condition of the patient. (*From* Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;49(1):1–45; with permission.)

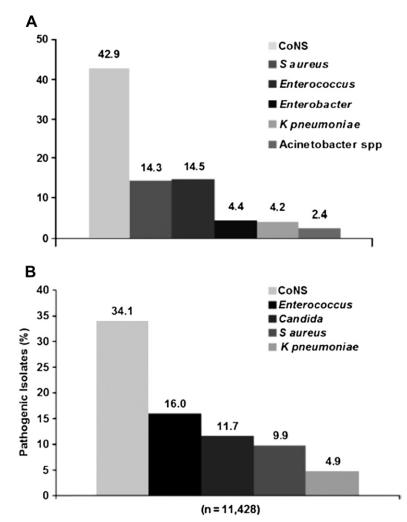


Fig. 4. Causative pathogens for CLABSI in US hospitals, 1986–2003 (*A*) versus 2006–2007 (*B*). Significant changes have been identified in CLABSI microbiology. Coagulase-negative *Staphylococci* remain the most common pathogen. In the NNIS report spanning 1986 to 2003, the next most common pathogens were *S aureus* and *Enterococci*, representing 14.3% and 14.5% of isolates, respectively. In the report from NHSN (2006–2007), *Enterococci* and *Candida* spp were the next most common, representing 16.0% and 11.7% of pathogens, respectively. These figures document a significant increase in *Candida* as causative pathogens for CLABSI and conversely, a significant reduction in *S aureus* isolates in the most recent period (from 14.3% to 9.9% of all pathogens). (*Data from* Hidron AI, Edwards JR, Patel J, et al. National Healthcare Safety Network Team Participating National Healthcare Safety Network Facilities. NHSN annual update: Antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. Infect Control Hosp Epidemiol 2008;29:996–1011.)

barrier precautions (cap, mask, sterile gown, sterile gloves, sterile full-body drape) during CVC insertion; (3) using a greater than 0.5% chlorhexidine skin preparation with alcohol for antisepsis; and (4) avoiding routine replacement of CVCs as a strategy to prevent infection. The use of antiseptic-impregnated (chlorhexidine/silver sulfadiazine) or antibiotic-impregnated (minocycline/rifampin) short-term CVCs¹³ and chlorhexidine-impregnated sponge dressings¹⁴ is recommended only if the CLABSI rate is not decreasing despite adherence to these initial strategies. These guidelines also emphasize performance improvement by documenting and reporting rates of compliance, with all components of the bundle as benchmarks for quality assurance and performance improvement. There has been a significant decline in ICU CLABSI rates in the United States (**Table 1**) related to prevention efforts.

VAP

Epidemiology

Hospital-acquired pneumonia (HAP) is the most common life-threatening HAI. Most are associated with mechanical ventilation (VAP), and associated with significant increases in length of ICU and hospital stay, mortality, and costs.¹⁵ VAP is a potentially life-threatening complication in surgical critical care.¹⁶ In a study of 554 critically ill trauma patients with VAP, patients with VAP alone had a case fatality rate of 12% versus a 26% case fatality rate in patients with concomitant bacteremia.¹⁷ Reports from the NHSN document a recent decline in VAP rates related to the implementation of prevention strategies. However, the highest rates of VAP remain in SICUs, particularly in burn and trauma ICUs (**Table 2**).¹⁸ VAP preventive strategies are therefore important to implement in all surgical patients.

Postoperative pneumonia incidence varies dependent on risk factors, ranging from an incidence of 1.5% to as high as 15.3% in high-risk groups. The 30-day postoperative mortality for all groups can be as high as 21%, dependent on the severity of illness, comorbidities, and causative pathogens.^{19,20} In a study of 48,247 adults who underwent colectomy with data available in the American College of Surgeons National Surgical Quality Improvement Program (2005–2008), postoperative pneumonia was significantly more common in patients undergoing emergent versus elective surgery (11.1% vs 2.9%) and decreased in the overall cohort over time (4.60% in 2005 to 3.97% in 2008).²¹

Pathophysiology

Both HAP and VAP are caused by introducing bacteria into the sterile lower respiratory tract. The pathogenesis of the bacteria is exacerbated by impaired host defenses. This bacterial introduction occurs by 2 important mechanisms: (1) bacterial colonization of the aerodigestive tract and (2) aspiration of contaminated secretions into the lower airway.^{22–25} Factors promoting the pathogenesis of VAP include the presence of invasive devices (endotracheal tube), medications altering gastric emptying and pH, and contaminated water, medications, and respiratory therapy equipment (**Fig. 5**).

VAP Clinical and Surveillance Definitions

Pneumonia is an acute infection of the pulmonary parenchyma. In 2005, the American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) provided guidelines to further categorize pneumonia into HAP (pneumonia occurring >48 hours after hospital admission), VAP (pneumonia that develops 48 hours after endotracheal intubation), and health care-associated pneumonia (HCAP) (**Fig. 6**).²⁶ HCAP is pneumonia that occurs in a patient with health care contact as defined by 1 or more of the

Table 1 Decline in CLABSI rates per 1000 central line days in ICUs in the United States (NHSN)

Type of ICU	2004 Pooled Mean ^a	2006 Pooled Mean ^b	2007 Pooled Mean ^c	2008 Pooled Mean ^d	2009 Pooled Mean ^e	2010 Pooled Mean/50% Median ^f
Burn	7.0	6.8	5.6	5.5	5.3	3.5/2.2
Medical: major teaching	5.0	2.9	2.4	2.6	2.2	1.8/1.4
Medical: all other	_	_	_	1.9	1.6	1.3/0.7
Medical cardiac	3.5	2.8	2.1	2.0	1.7	1.3/0.9
Medical/surgical: major teaching	4.0	2.4	2.0	2.1	1.7	1.4/1.0
Medical/surgical: all other, <15 beds	3.2	2.2	1.5	1.5	1.4	1.1/0.0
Medical/surgical: all other, >15 beds	_	_	_	1.5	1.3	1.0/0.8
Neurologic	_	-	1.2	1.4	1.8	1.2/0.6
Neurosurgical	4.6	3.5	2.5	2.5	1.5	1.3/0.8
Pediatric cardiothoracic	_	_	_	3.3	2.5	2.1/1.7
Pediatric medical	_	_	1.0	1.3	2.6	1.9/1.9
Pediatric medical/surgical	6.6	5.3	2.9	3.0	2.2	1.8/1.4
Surgical: major teaching	4.6	2.7	2.3	2.3	1.8	1.4/1.0
Surgical: all other				_	_	1.0/0.6
Surgical cardiothoracic	2.7	1.6	1.4	1.4	1.2	0.9/0.6
Trauma	7.4	4.6	4.0	3.6	2.6	1.9/1.5

^a NNIS System Report, data summary from January 1992 through June 2004, issued October 2004. Am J Infect Control 2004;32:470–485.

^b Edwards JR, Peterson KD, Andrus ML, et al. National Healthcare Safety Network (NHSN) Report, data summary for 2006, issued June 2007. Am J Infect Control 2007;35:290–301.

^c Edwards JR, Peterson KD, Andrus ML, et al. National Healthcare Safety Network (NHSN) Report, data summary for 2006 through 2007, issued November 2008. Am J Infect Control 2008;36:609–26.

^d Edwards JR, Peterson KD, Mu Y, Banerjee S, Allen-Bridson K, Morrell G, Dudeck MA, Pollock DA, Horan TC. National Healthcare Safety Network (NHSN) report: data summary for 2006 through 2008, issued December 2009. Am J Infect Control 2009;37(10):783–805.

^e Dudeck MA, Horan TC, Peterson KD, Allen-Bridson K, Morrell GC, Pollock DA, Edwards JR. National Healthcare Safety Network (NHSN) report, data summary for 2009, device-associated module. Am J Infect Control 2011;39(5):349–67.

^f Dudeck MA, Horan TC, Peterson KD, Allen-Bridson K, Morrell G, Pollock DA, Edwards JR. National Healthcare Safety Network (NHSN) Report, data summary for 2010, device-associated module. Am J Infect Control 2011;39(10):798–816.

Table 2

Decline in VAP cases per 1000 ventilator days in ICUs in the United States. (Note higher VAP rates in surgical and neurosurgical ICUs and highest rates in burn and trauma ICUs.)

Type of ICU	2004 Pooled Mean ^a	2006 Pooled Mean ^b	2007 Pooled Mean ^c	2008 Pooled Mean ^d	2009 Pooled Mean ^e	2010 Pooled Mean/ 50% Median ^f
Burn	12.0	12.3	10.7	10.7	7.4	5.8/3.3
Medical: major teaching	4.9	3.1	2.5	2.4	1.9	1.4/1.0
Medical: all other	_	_	_	2.2	1.4	1.0/0.0
Medical cardiac	4.4	2.8	2.5	2.1	1.5	1.3/0.0
Medical/surgical: major teaching	5.4	3.6	3.3	2.9	2.0	1.8/1.1
Medical/surgical: all other, \leq 15 beds	5.1	2.7	2.3	2.2	1.4	1.2/0.0
Medical/surgical: all other, >15 beds		_	-	1.9	1.2	1.1/0.3
Neurologic		-	7.1	6.7	3.9	4.8/4.8
Neurosurgical	11.2	7.0	6.5	5.3	3.8	3.1/2.3
Pediatric cardiothoracic	-	-	-	0.6	0.7	0.7
Pediatric medical	_	-	-	2.3	0.9	1.1
Pediatric medical/surgical	2.9	2.5	2.1	1.8	1.1	1.2/0.0
Surgical: major teaching	9.3	5.2	5.3	4.9	3.8	3.5/1.7
Surgical: all other		_	_			2.5/1.2
Surgical cardiothoracic	7.2	5.7	4.7	3.9	2.1	1.6/0.4
Trauma	15.2	10.2	9.3	8.1	6.5	6.0/5.3

^a NNIS System Report, data summary from January 1992 through June 2004, issued October 2004. Am J Infect Control 2004;32:470–485.

^b Edwards JR, Peterson KD, Andrus ML, et al. NHSN Facilities. National Healthcare Safety Network (NHSN) Report, data summary for 2006, issued June 2007. Am J Infect Control 2007;35:290–301.

^c Edwards JR, Peterson KD, Andrus ML, et al. National Healthcare Safety Network Facilities. National Healthcare Safety Network (NHSN) Report, data summary for 2006 through 2007, issued November 2008. Am J Infect Control 2008;36:609–26. Erratum in: Am J Infect Control 2009;37:425.

^d Edwards JR, Peterson KD, Mu Y, Banerjee S, Allen-Bridson K, Morrell G, Dudeck MA, Pollock DA, Horan TC. National Healthcare Safety Network (NHSN) report: data summary for 2006 through 2008, issued December 2009. Am J Infect Control 2009;37(10):783–805.

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^f Dudeck MA, Horan TC, Peterson KD, Allen-Bridson K, Morrell G, Pollock DA, Edwards JR. National Healthcare Safety Network (NHSN) Report, data summary for 2010, device-associated module. Am J Infect Control 2011;39(10):798–816.

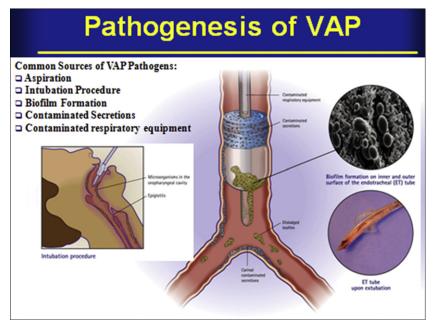


Fig. 5. Pathway of colonization of airway in VAP.

following criteria: a patient hospitalized for 2 days or more in an acute care facility within 90 days of infection; a patient residing in a nursing home or long-term care facility; a patient who has attended a hospital or hemodialysis center; a patient who has received intravenous antibiotic therapy, chemotherapy, or wound care within

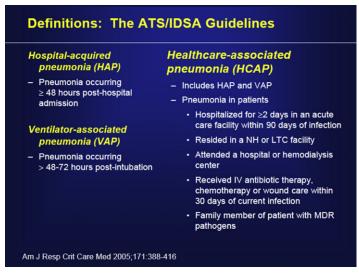


Fig. 6. ATS/IDSA Guideline: pneumonia definitions. (*Data from* American Thoracic Society. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171(4):388–416.)

30 days of the current infection; and any patient who is a family member of a patient with a multidrug-resistant (MDR) pathogen.

The CDC NHSN VAP definition for surveillance (last updated in 2002) uses a combination of radiologic, clinical, and laboratory criteria in patients who are ventilated for greater than 48 hours. Three components make up the current pneumonia (PNEU) definitions: an "X-ray" component (required), a "Signs and symptoms" component (required), and a "Laboratory" component (optional). Pneumonia is characterized into 3 types including clinically defined pneumonia (PNEU-1), common bacterial, fungal, or atypical pneumonia (PNEU-2), and pneumonia in immunocompromised patients (PNEU-3) (Fig. 7). The diagnosis requires new or progressive and persistent infiltrate/consolidation/cavitation on 2 or more serial chest radiographs. In addition, it must meet minimum criteria in 2 separate clinical categories (Fig. 8) and minimum criteria in laboratory categories (Fig. 9).

The CDC has recommended a significant change to VAP surveillance in the United States. A VAP Surveillance Definition Working Group was convened in September 2011 by the CDC's Division of Healthcare Quality Promotion in collaboration with the CDC Prevention Epicenters, the Critical Care Societies Collaborative (http:// ccsconline.org), other professional societies, subject matter experts, and federal partners. There is currently no gold-standard, valid, reliable definition for VAP. Therefore, the Working Group pursued a different approach: development of a surveillance definition algorithm for detection of ventilator-associated events (VAEs). This algorithm detects a broad range of conditions or complications occurring in mechanically ventilated adult patients. The Working Group focused on definition criteria that use objective, clinical data expected to be readily available across the spectrum of mechanically ventilated patients. These criteria are less likely to be influenced by variability in resources, subjectivity, and clinical practices and are potentially amenable to electronic data capture. The proposed algorithm to detect VAEs in adult patients serves a surveillance function and is not designed for use in the clinical care of patients.²⁷

CDC / NNIS Definition of VAP: 2002					
Pneumonia I:	Clinically defined Pos. serial X-ray finding and				
	One category I and two category II clinical signs				
Pneumonia II:	Common bacterial / fungal pneumonia				
	Pos. serial X-Ray finding <u>and</u>				
	One category I <u>and</u> one category II clinical signs <u>and</u> One category I or II laboratory finding				
Pneumonia II:	Atypical pneumonia				
	Pos. serial X-Ray finding and				
	One category I <u>and</u> one category II clinical signs <u>and</u> One category III laboratory finding				
Pneumonia III	Immunocompromised patient				
	Pos. serial X-Ray finding and				
	One category I <u>or</u> II clinical sign <u>and</u> One category I, II or III laboratory finding				

Fig. 7. CDC definition of VAP: PNEU-1, PNEU-2, PNEU-3 definitions.

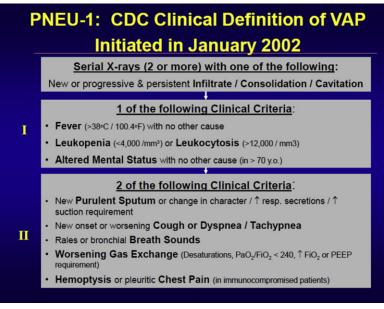


Fig. 8. CDC clinical definition of VAP for PNEU-1.

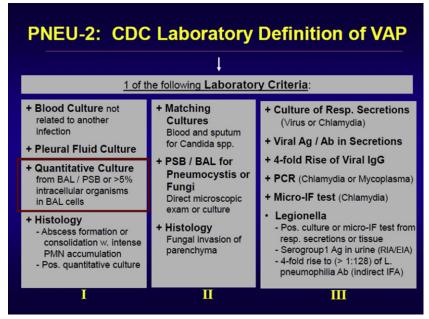


Fig. 9. CDC definition of VAP for PNEU-2 - one laboratory criteria required.

Diagnosis

The diagnosis of VAP is difficult because the clinical findings are nonspecific and the differential diagnosis can be broad.²⁸ When findings at autopsy are used as a reference, the combination of radiographic infiltrate plus 2 of 3 clinical features (fever >38°C, leukocytosis/leukopenia, purulent secretions) resulted in 69% sensitivity and 75% specificity for pneumonia.²⁹ Only 43% of patients with radiographic evidence of infiltrate were found to have VAP by postmortem examination.³⁰

When VAP is suspected, we recommend diagnostic lower respiratory tract sampling for microscopic evaluation and quantitative culture, which can be performed with flexible bronchoscopy (bronchoalveolar lavage [BAL]) or without bronchoscopy (mini-BAL) with similar safety and diagnostic accuracy.³¹ In patients with left lower lobe infiltrates and possible VAP, bronchoscopic BAL is preferred to obtain a sample from this area, because mini-BAL sampling catheters most commonly advance into the right lower lobe bronchus. Bronchoscopic sampling is not associated with improved mortality, or reduced duration of ventilation or ICU or hospital length of stay. However, it does influence antibiotic selection and de-escalation of antibiotics.³²

Given the severity of VAP and the frequency of serious conditions that can mimic VAP, additional tests that provide further evidence for VAP are clearly warranted.³³ At present, no sensitive and specific biomarker is currently available to confirm a VAP diagnosis. C-reactive protein, procalcitonin, and soluble triggering receptor expressed on myeloid cells (sTREM-1, a member of the immunoglobulin superfamily whose expression on phagocytes is specifically upregulated by microbial products) have been evaluated as biomarkers for diagnosing VAP. Multiple studies have confirmed that C-reactive protein and procalcitonin have poor diagnostic value for VAP.^{34–36} Additional studies have confirmed conflicting results for sTREM-1.^{37–40}

Treatment

Early empiric broad-spectrum antimicrobial therapy for VAP should be initiated, ideally after obtaining lower respiratory tract quantitative cultures. An assessment of clinical response and cultures over the next 48 hours is imperative. If there is clinical improvement and culture results are negative, consider stopping antibiotics. If culture results are positive, consider de-escalating or narrowing the antibiotics based on sensitivities. If there is no clinical response, consider searching for other causes. If cultures are negative, assess for other pathogens, complications, or other sources of infection. If cultures are positive, adjust antibiotic therapy and search for other sources as well. An algorithm for diagnosis and treatment of pneumonia provided by the ATS/IDSA 2005 guidelines is shown in **Fig. 10**.

Specific Antibiotic Treatment

The initiation of early, appropriate empiric antibiotics to treat VAP significantly improves patient survival.⁴¹ The microbiology of VAP has changed over the past decade (**Fig. 11**). For years (1992–1999), *S aureus* and *Pseudomonas aeruginosa* were the 2 leading causative pathogens for VAP, each representing approximately 18% of all isolates. *Enterobacter* spp and *Klebsiella pneumoniae* were less common, comprising 12% and 7% of VAP isolates, respectively.^{42,43} The most recent NHSN report (2006–2007) for VAP confirms a significant change in VAP pathogens.⁴⁴ *S aureus* is now the leading VAP pathogen, representing 24.4% of all isolates, with 54.4% confirmed as MRSA, making MRSA the leading VAP pathogen. In the 2007 EPIC II point-prevalence study of infection in critically ill patients performed on May 8, 2007, MRSA infection in ICU patients was independently associated with an almost

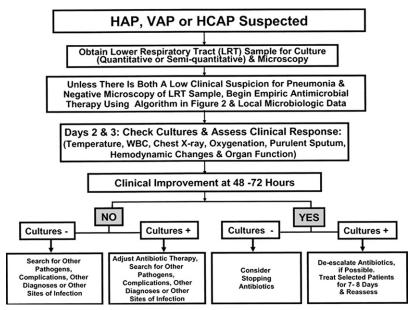


Fig. 10. Algorithm for diagnosis and treatment of suspected HAP, VAP, or HCAP. (*Reprinted with permission of* the American Thoracic Society. Copyright © 2012 American Thoracic Society. American Thoracic Society. Guidelines for the management of adults with hospital acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171(4):388–416. Official journal of the American Thoracic Society. This document was published in 2005 and is currently in revision. Certain aspects of this document may be out of date and caution should be used when applying it to patient care.)

50% higher likelihood of hospital death compared with methicillin-sensitive *S* aureus (MSSA) infection, and the most common site of infection was the respiratory system.⁴⁵ *Pseudomonas aeruginosa* decreased from 18% to 16.3% and *Enterobacter* decreased from 12% to 8.4%. *Acinetobacter baumanii* is now the third most common VAP pathogen, comprising 8.4% of all VAP isolates. This MDR pathogen is difficult to eradicate, and is a significant issue for infection control. Empiric antibiotics for VAP should cover these potential causative pathogens, and knowledge of the local ICU antibiogram is important in antibiotic choice.⁴⁶

Necrotizing pneumonias are an increasing problem and are associated with a higher mortality in our critically ill patients. Pathogens associated with necrotizing pneumonia include *Pseudomonas* and MRSA. Concurrent with the emergence of community-associated MRSA (CA-MRSA), there are increasing reports of community-acquired necrotizing pneumonia in young healthy patients, some after a viral prodrome and influenza infection.^{47,48} In the most recent report from the CDC of 51 cases of *S aureus* community-acquired pneumonia, median age was 16 years and 44% had no underlying comorbidities. Influenza was confirmed in 33% of the cohort, and 91% of these patients died. MRSA was confirmed in 37 of the 51 patients and 48% died. Empiric coverage for MRSA pneumonia was provided in only 43% of these patients.⁴⁹

Concomitant use of antibiotics that suppress toxin production is advocated for the treatment of severe and invasive CA-MRSA infections, including pneumonia. The rationale for their use in CA-MRSA pneumonia includes (1) the presumed role of the Panton-Valentine leukocidin (PVL) toxin, a staphylococcal toxin known to be associated with tissue necrosis,⁵⁰ and (2) the high morbidity and mortality observed.

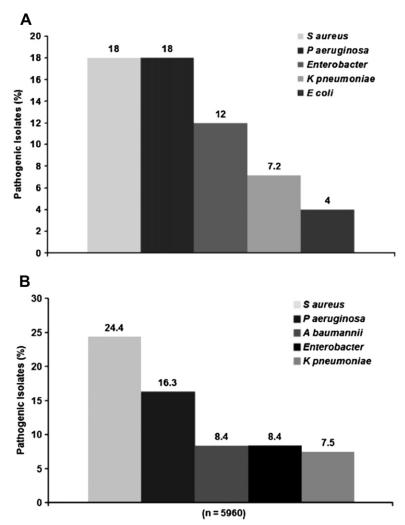


Fig. 11. Causative pathogens for VAP in US hospitals. (A)1992–1999 versus (B) 2006–2007 NHSN Report. *S aureus* increased from 18% to 24.4%. MRSA is now the leading causative pathogen, comprising 54.4% of all *S aureus* isolates. Note higher rate of *Acinetobacter* in 2006–2007. (*Data from* Hidron AI, Edwards JR, Patel J, et al. National Healthcare Safety Network Team Participating National Healthcare Safety Network Facilities. NHSN annual update: Antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. Infect Control Hosp Epidemiol 2008;29:996–1011.)

Some therefore advocate treatment with agents that suppress toxin production (clindamycin, linezolid) and urge the avoidance of agents (ie, β -lactams) that can lead to increased production of PVL and other exotoxins in patients with MRSA pneumonia.⁵¹

The choice of antibiotic treatment in VAP depends on the microorganism isolated. These organisms differ based on duration of mechanical ventilation. Patients who develop VAP early (<4 days of mechanical ventilation) have different isolates than those who develop VAP later (>4 days).²² The usual pathogens in early VAP are *S*

aureus (MSSA), Haemophilus influenzae, and Streptococcus pneumoniae. These pathogens tend to be sensitive to antimicrobial therapy. The pathogens in late VAP tend to be gram negative and MDR. Usual isolates include Pseudomonas aeruginosa, Acinetobacter baumanii, S aureus (MRSA), and Stenotrophomonas maltophilia.⁵² The antibiotic should be selected based on risk factors for MDR bacteria. Risk factors in addition to duration of mechanical ventilation include recent antibiotic therapy, presence of underlying diseases, sensitivities of hospital or ICU organisms, and the possibility of HCAP. Rapid initiation of appropriate antibiotic therapy in VAP is associated with improved outcome. Inadequate antibiotic therapy is a strong predictor of death in patients with VAP, irrespective of underlying disease state and severity of illness.53-56 Risk factors for inadequate antimicrobial treatment in VAP were MDR bacteria, polymicrobial infection, and late-onset VAP.⁵⁷ To avoid inadequate antibiotic therapy, early use of empiric broad-spectrum antibiotics to cover all potential causative pathogens is required. Empiric antibiotics for pneumonia should be based on national guidelines and with consideration of local antibiograms (Box 2). Antibiotics are started when a clinical diagnosis is made immediately after cultures are obtained. Antibiotics are modified to a more narrow spectrum (de-escalation) as soon as possible based on culture and susceptibility results.

The 2005 ATS/IDSA guidelines provide recommendations for empiric antibiotics for VAP. Patients with no risk factors for MDR bacteria are treated with ceftriaxone, quinolones, ampicillin-sulbactam, or ertapenem. Patients with late-onset pneumonia (>5 days) or those with risk factors for MDR bacteria must be treated with a broader spectrum of antibiotics. Particular attention is paid to starting initial combination therapy for possible gram-negative infection (because *Pseudomonas* is most common, 2 agents are recommended so that at least 1 agent may have appropriate susceptibility), with concomitant coverage of gram-positive/MRSA infection (**Fig. 12**). A study of 924 episodes of suspected VAP suggested that negative active surveillance cultures for MRSA (from nares, oropharynx, or trachea, and any open wound) performed on ICU admission can accurately exclude MRSA as a cause in most patients with VAP, decreasing the need for empiric MRSA coverage.⁵⁸ These data from a single center must be validated in additional trials.

Box 2

Risk factors for MDR pathogens causing HAP, HCAP, and VAP

- Antimicrobial therapy in preceding 90 days
- Current hospitalization of 5 days or more
- High frequency of antibiotic resistance in the community or in the specific hospital unit
- Presence of risk factors for HCAP:

Hospitalization for 2 days or more in the preceding 90 days

Residence in a nursing home or extended care facility

Home infusion therapy (including antibiotics)

Chronic dialysis within 30 days

Home wound care

Family member with MDR pathogen

Immunosuppressive disease or therapy

Data from American Thoracic Society. Guidelines for the management of adults with hospitalacquired, ventilator-associated, and health care-associated pneumonia. Am J Respir Crit Care Med 2005;171(4):388–416.

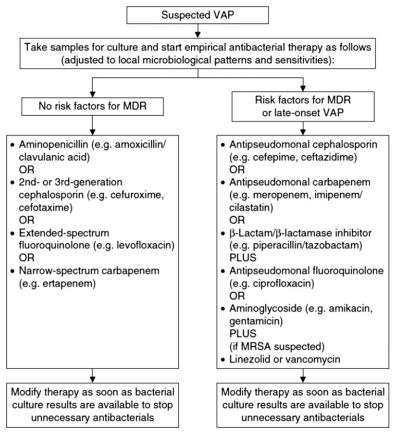


Fig. 12. Initial empiric antibiotic therapy for HAP, VAP, and HCAP with risk for MDR pathogens. (*Data from* American Thoracic Society. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171(4):388–416.)

Duration of Antibiotics for VAP

A landmark prospective, randomized multicenter trial compared 8 versus 15 days of antibiotic treatment of VAP in 401 patients in 51 ICUs.⁵⁹ No difference in 30-day mortality was identified (18.8% vs 17.2%) and no differences in ventilator-free days, organ failure-free days, length of ICU stay and 60-day mortality were identified. However, there was a higher recurrence of infection rate for nonfermenting gram-negative bacilli, including *Pseudomonas aeruginosa*. In addition, more MDR pathogens appeared in the 15-day treatment group (42% vs 62%, P = .038). Based on the results of this study, optimal duration of therapy for VAP should be 8 days, except in those isolates that are nonfermenting gram-negative bacilli, including *Pseudomonas aeruginosa* and *Acinetobacter* species, for which longer duration of antimicrobial therapy is recommended.

However, the duration of antimicrobial therapy for VAP caused by MRSA needs additional evaluation, because the studies that evaluated treatment duration included an insufficient number of MRSA-infected patients. Most clinicians provide a minimum of 14 days of therapy for MRSA pneumonia, and if there is concomitant bacteremia, more prolonged antibiotic therapy may be required. Duration of antimicrobial therapy should be assessed according to each patient's clinical course as well.

VAP Prevention

The foremost strategy for VAP prevention is to avoid intubation or reduce time of duration of mechanical ventilation. Noninvasive ventilation may be particularly valuable because it can lead to avoidance of intubation or shortening the duration of mechanical ventilation, therefore noninvasive ventilation should be considered when evidence exists to support its use.⁶⁰ Basic infection control principles like hand washing, adequate ICU staff education, and optimal resource use are necessary. The strategies to prevent infection include (1) reducing bacterial colonization of the aerodigestive tract and (2) decreasing aspiration of contaminated secretions into the lower airway. Decreasing aspiration incidence is achieved through semirecumbent positioning, and use of specialty endotracheal tubes that aspirate subglottic secretions. Bacterial colonization is reduced by minimizing the days on mechanical ventilation through weaning protocols, use of chlorhexidine in the posterior pharynx and silver-coated endotracheal tubes. Clinical guidelines for VAP prevention review all evidence-based strategies for VAP prevention.⁶¹ Ventilator bundles are used as an effective method to reduce VAP rates in the ICU.⁶²

Semirecumbent position

The semirecumbent (45°) position in mechanically ventilated patients is associated with a reduced incidence of VAP. A prospective randomized trial with 86 patients found a significant difference in the incidence of VAP (34% supine vs 3% head of the bead at 45°, P = .003).⁶³ Supine position and mechanical ventilation greater than 7 days were both independent risk factors for VAP. Other studies have not confirmed this finding, but compliance with the target semirecumbent position was not reached in these studies.^{64,65}

Continuous aspiration of subglottic secretions endotracheal tubes

Aspirated secretions may pool above the endotracheal cuff and increase the risk for VAP. Specialty tubes that provide continuous aspiration of subglottic secretions (CASS) are commercially available. Several prospective randomized trials show a decreased VAP rate of VAP with CASS endotracheal tubes. A meta-analysis of 5 studies with 896 patients showed a reduction of VAP by nearly half (relative risk [RR] = 0.51), and delayed the onset of VAP by 6.8 days and reduced ICU length of stay by 3 days. Despite these beneficial outcomes, no improvement in mortality was identified. A study in cardiac surgical patients (n = 714) also confirmed a significant VAP reduction with use of the CASS tube.⁶⁶ The CASS tube is ideal for patients who are expected to require mechanical ventilation greater than 72 hours, but this may be difficult to predict.⁶⁷ Management of CASS tubes requires particular attention to detail for maintenance, frequent monitoring, and their use is associated with increased cost.⁶⁸

Chlorhexidine gluconate

One strategy to reduce bacterial colonization of the aerodigestive tract is the use of oral chlorhexidine gluconate (0.12%). One trial in cardiac surgical patients documented a significant decrease in the incidence of nosocomial pneumonia and mortality.⁶⁹ A prospective, randomized, double-blind, placebo-controlled, multicenter trial also confirmed a significant reduction in VAP with use of chlorhexidine.⁷⁰ A meta-analysis of similar trials concluded that the use of chlorhexidine was associated with a 26% RR reduction in VAP.⁷¹ In addition, it has also been shown that use of chlorhexidine in combination with protocol-driven weaning from mechanical ventilation reduces the incidence of VAP in SICU patients.⁷² The addition of manual tooth-brushing to chlorhexidine oral care does not help to prevent VAP.^{73,74}

Silver-coated endotracheal tube

Another strategy to reduce bacterial colonization is the use of silver-coated endotracheal tubes. Silver prevents biofilm formation, delays airway colonization, has bactericidal activity, and reduces bacterial burden. The North American Silver-Coated Endotracheal Tube (NASCENT) randomized single-blind multicenter phase III trial enrolled 2003 patients expected to require mechanical ventilation for more than 24 hours. The primary outcome measure was VAP (defined as BAL >10⁴ CFU/mL). Use of the silver-coated endotracheal tube was associated with a significant VAP reduction (4.8% vs 7.5%, RR 36%) and was associated with a significant delay in time to VAP.⁷⁵

Spontaneous awakening and breathing trials

Prolonged mechanical ventilation is a risk factor for VAP, which increases by 1% to 3% with each day of mechanical ventilation.⁷⁶ The use of a weaning protocol, a sedation protocol, or both has been shown to reduce the duration of mechanical ventilation.⁷⁷ The Awakening and Breathing Controlled (ABC) trial enrolled 336 patients requiring mechanical ventilation at 4 tertiary care hospitals. The group was divided into an intervention group (n = 168), who received daily spontaneous awakening trials (SATs) and spontaneous breathing trials (SBTs), and a control group (n-168), who received sedation and usual care with SBTs. The study found a significant difference in 1-year mortality between the control and intervention group (58% vs 44%, P = .01). Routine use of SAT and SBT should be standard in all mechanically ventilated patients.

Selective decontamination

Selective decontamination of the digestive tract and oropharynx are strategies aimed at preventing colonization with virulent bacteria. The spectrum of studies includes oral administration of antibiotics via nasogastric tubes and intravenous administration for up to 4 days.⁷⁸ Several studies have shown modest benefit in pneumonia rate and mortality.^{79,80} However, this modality has not been used widely in the United States because of significant concern about potential emergence of MDR bacteria.⁸¹

Tracheostomy

Previous studies have suggested that tracheostomy was superior to prolonged intubation for VAP prevention,⁸² but 2 recent large, prospective, randomized clinical trials have found no difference in VAP or any other outcomes measures comparing early (6–8 days) versus late (13–15 days) tracheostomy in 419 patients⁸³ or comparing early (4 days) versus late (after 10 days) in 909 patients in the TracMan trial.⁸⁴ Thus, early tracheostomy should not be performed for VAP prevention, but may be considered for other reasons, such as patient comfort and airway protection, as in patients with severe traumatic brain injury.

CA-UTI Enidomio

Epidemiology

UTIs are the most common HAI in acute care hospitals in the United States, and account for approximately 23% of nosocomial infections in the ICU; of these, 97% are CA-UTI.⁸⁵ Each year, there are more than 500,000 cases of CA-UTIs in the United States, accounting for 30% or more of HAIs.⁸⁶ Although not directly linked with mortality, CA-UTIs are associated with approximately 20% of hospital-acquired bacteremia, which in turn has a mortality of 10%.⁸⁷

Risk Factors

The most important risk factors for the development of a CA-UTI are the presence and duration of a urinary catheter. The incidence of catheter-associated bacteriuria (CA bacteriuria) is 3% to 8% per day of indwelling catheter.^{88,89} Urinary catheters are used in 15% to 25% of all hospitalized patients, and 5% to 10% of nursing home residents. Often these catheters are placed for inappropriate indications and are not removed in a timely fashion. In 1 survey of US hospitals, more than 50% of physicians did not monitor which patients were catheterized and more than 75% did not monitor the durations or discontinuation of indwelling catheters.⁹⁰ This situation leads to increased risk for bacteriuria. Other risk factors include female gender, obesity, immunodeficiency, and length of stay in an ICU.⁹¹

Diagnosis

The CDC distinguishes between symptomatic UTI (SUTI) and asymptomatic bacteriuria (ASB) according to defined criteria listed in **Box 3** and **Table 3**.⁹² Patients with SUTI have 1 or more of the following symptoms: fever, rigors, altered mental status, malaise, or lethargy with no other identified cause, flank pain, costovertebral angle tenderness, acute hematuria, pelvic discomfort, dysuria, urgency or frequency of urination, suprapubic pain or tenderness, or in the case of patients with spinal cord injury, increased spasticity, autonomic dysreflexia, or sense of unease. UTIs are considered CA-UTI if the patient has an indwelling urethral or suprapubic catheter, undergoes intermittent self-catheterization (ISC), or had removal within the last 48 hours or less of a urethral, suprapubic, or condom catheter. By contrast, catheterassociated ASB (CA-ASB) is defined as the presence of 10⁵ cfu/mL or more of 1 or more bacterial species in a single catheter urine specimen in a patient without UTI symptoms. Pyuria is not a distinguishing factor between CA-UTI and CA-ASB, and should not be used as an indication for antimicrobial therapy.

Treatment

Patients with indwelling catheters should not undergo routine screening and treatment of ASB, with the exception of pregnant women and patients who undergo urologic procedures for which visible mucosal bleeding is anticipated. Women who have had short-term indwelling catheters with persistent CA-ASB for 48 hours or more after catheter removal may be considered for antimicrobial treatment; data are insufficient to make recommendations in men. Urine cultures should be obtained before initiating antimicrobial therapy for presumed CA-UTI and tailored to specific organisms based on culture results. For indwelling catheters present for 2 weeks or more, catheter replacement may hasten resolution of symptoms. If the catheter can be removed, then a midstream voided urine specimen should be obtained for urine culture before initiation of antimicrobial treatment. Length of treatment should be tailored to specific clinical scenarios. In women 65 years old or younger without upper urinary tract symptoms, a 3-day regimen should be sufficient. In patients who are not severely ill and have CA-UTI, 5 to 7 days of antimicrobial coverage is recommended for prompt resolution of symptoms; 10 to 14 days of treatment is recommended for patients with delayed resolution of symptoms.

Prevention

Effective from January 1, 2012, the Joint Commission's Board of Commissioners approved a new National Patient Safety Goal regarding CA-UTIs for hospitals in the United States (**Table 4**).^{93,94} These goals reflect the guidelines set forth by the IDSA for the diagnosis, prevention, and treatment of CA-UTIs. As to be expected, the best prevention is limiting catheter use to only clear indications (**Box 4**), with prompt catheter removal as soon as it is no longer necessary. Condom catheters may be considered in men who have minimal postvoid residual volume, but there are insufficient data to suggest that these decrease UTI rates compared with indwelling catheters.

Box 3

Definitions of CA-UTI (SUTI and ASB) in adults under the NNIS system and the NHSN through December 2008

Catheter-associated SUTI must meet at least 1 of the following 2 criteria:

- 1. Criterion 1:
 - a. Patient has had an indwelling urinary catheter within 7 days before the culture; and
 - b. Patient has at least 1 of the following signs or symptoms with no other recognized cause: fever (temperature, >38°C), urgency, frequency, dysuria, or suprapubic tenderness; and
 - c. Patient has a positive urine culture result (ie, $\geq 10^5$ microorganisms/mL of urine with no more than 2 species of microorganisms).
- 2. Criterion 2:
 - a. Patient has had an indwelling urinary catheter within 7 days before the culture; and
 - b. Patient has at least 2 of the following signs or symptoms with no other recognized cause: fever (temperature, >38°C), urgency, frequency, dysuria, or suprapubic tenderness; and
 - c. Patient has at least 1 of the following:
 - i. Positive dipstick result for leukocyte esterase or nitrate;
 - ii. Pyuria (urine specimen with \geq 10 WBCs/mm³ or 3 \geq WBCs/high-power field of unspun urine);
 - iii. Organisms seen on Gram stain of unspun urine;
 - iv. At least 2 urine cultures with repeated isolation of the same uropathogen (gramnegative bacteria or *Staphylococcus saprophyticus*) with $\geq 10^2$ colonies/mL in nonvoided specimens;
 - v. Concentration of $\leq 10^5$ colonies/mL for a single uropathogen (gram-negative bacteria or S saprophyticus) in a patient being treated with an effective antimicrobial agent for a UTI;
 - vi. Physician diagnosis of a UTI;
 - vii. Physician institutes appropriate therapy for a UTI.

CA-ASB must meet the following criteria:

- 1. Patient has had an indwelling urinary catheter within 7 days before the culture; and
- 2. Patient has a positive urine culture result (ie, $\geq 10^5$ microorganisms/mL of urine with no more than 2 species of microorganisms); and
- 3. Patient has no fever (temperature, >38°C), urgency, frequency, dysuria, or suprapubic tenderness.

Abbreviation: WBC, white blood cell.

Data from Burton DC, Edwards JR, Srinivasan A, et al. Trends in catheter-associated urinary tract infections in adult ICUs-United States, 1990-2007. Infect Control Hosp Epidemiol 2011;32(8):748–56. PubMed PMID: 21768755.

ISC should be considered an alternative to indwelling catheters to reduce CA-UTI. There are fewer associated complications to ISC compared with indwelling Foley catheters, and some advantages include fewer instances of CA-ASB, pyelonephritis, epididymitis, periurethral abscess, urethral stricture, vesicoureteral reflux, hydronephrosis, bladder and renal calculi, bladder cancer, and autonomic dysreflexia. A recent Cochrane review of randomized and quasirandomized trials

Table 3 Risk factors for development of CA-UTI, symptomatic versus asymptomatic					
SUTI	Bacteriuria				
Prolonged catheterization ^a	Disconnection of drainage system ^a				
Female sex ^b	Lower professional training of inserter ^a				
Older age ^b	Placement of catheter outside the operating room ^b				
Impaired immunity ^b	Incontinence ^b Diabetes Meatal colonization Renal dysfunction Orthopedic/neurology services				

^a Main modifiable risk factors.

^b Also inform recommendations. Available at: http://www.cdc.gov/HAI/pdfs/toolkits/CAUTItoolkit_3_10.pdf.

comparing indwelling Foley catheters versus ISC for surgical patients with short-term bladder drainage (defined as \leq 14 days' duration) found that there were significantly more cases of CA-ASB in the indwelling Foley catheter group (RR, 2.90; 95% confidence interval, 1.44–5.84).⁹⁵

Table 4 Performance measures approved by the Joint Commission on Accreditation Organizations as a National Patient Safety Goal (NPSG) for 2012	on of Healthcare
Requirement	Level of Evidence
EP2: Insert indwelling urinary catheters according to established evidence-based guidelines that address the following:	
Limiting use and duration to situations necessary for patient care	A-II
Using aseptic techniques for site preparation, equipment, and supplies	A-III
EP3: Manage indwelling urinary catheters according to established evidence-based guidelines that address the following:	
Securing catheters for unobstructed urine flow and drainage	A-III
Maintaining the sterility of the urine collection system	A-I
Replacing the urine collection system when required	B-III
Collecting urine samples	A-III
EP4: Measure and monitor CA-UTI prevention processes and outcomes in high-volume areas by doing the following:	
Selecting measures using evidence-based guidelines or best practices	A-II or B-II for all
Monitoring compliance with evidence-based guidelines or best practices	
Evaluating the effectiveness of prevention efforts	
Note: Surveillance may be targeted to areas with a high volume of patients using indwelling catheters. High-volume areas are identified through the hospital's risk assessment as required in IC.01.03.01, EP 2	B-III

NPSG.07.06.01: Implement evidence-based practices to prevent indwelling CAUTI.^a

Note: This NPSG is not applicable to pediatric populations. Research resulting in evidence-based practices was conducted with adults, and there is not consensus that these practices apply to children.

^a Evidence-based guidelines for CA-UTI are located at: Compendium of Strategies to Prevent Healthcare-Associated Infections in Acute Care Hospitals at, http://www.shea-online.org/about/ compendium.cfm Guideline for Prevention of Catheter-associated Urinary Tract Infections, 2009 at http://www.cdc.gov/hicpac/cauti/001_cauti.html.

Available at: http://www.jointcommission.org/assets/1/18/r3_report_issue_2_9_22_11_final.pdf.

Box 4

Examples of appropriate and inappropriate indications for indwelling urethral catheter use (Note: these indications are based primarily on expert consensus)

Examples of appropriate indications for indwelling urethral catheter use

Patient has acute urinary retention or bladder outlet obstruction

Need for accurate measurements of urinary output in critically ill patients

Perioperative use for selected surgical procedures:

Patients undergoing urologic surgery or other surgery on contiguous structures of the genitourinary tract

Anticipated prolonged duration of surgery (catheters inserted for this reason should be removed in postanesthesia care unit)

Patients anticipated to receive large-volume infusions or diuretics during surgery

Need for intraoperative monitoring of urinary output

To assist in healing of open sacral or perineal wounds in incontinent patients

Patient requires prolonged immobilization (eg, potentially unstable thoracic or lumbar spine, multiple traumatic injuries such as pelvic fractures)

To improve comfort for end-of-life care if needed

Examples of inappropriate uses of indwelling catheters

As a substitute for nursing care of the patient or resident with incontinence

As a means of obtaining urine for culture or other diagnostic tests when the patient can voluntarily void

For prolonged postoperative duration without appropriate indications (eg, structural repair of urethra or contiguous structures, prolonged effect of epidural anesthesia)

Equipment

For intermittent catheterization, clean (nonsterile) technique may be considered with no difference in risk of CA-ASB or CA-UTI. However, indwelling urethral catheters should be inserted using aseptic (sterile) technique and with sterile equipment. Current data do not support the routine use of coated hydrophilic versus uncoated catheters, and further studies need to be conducted before any conclusion can be made.⁹⁶ A closed catheter drainage system with ports in the distal catheter for needle aspiration should be used and institution-specific strategies developed to ensure that disconnection of the catheter junction is minimized. The drainage bag is always kept below the level of the bladder. Preconnected Foley insertion systems may be considered but no data exist that this reduces CA-UTI. However, use of complex closed drainage system or application of tape at the catheter–drainage tube junction is not recommended.

Systems approach

Unit-wide and hospital-wide policies may be useful in infection prevention. More than 56% of hospitals do not have a system in place for monitoring patients with Foley catheters, and 74% do not monitor duration of catheterization. Shortened duration of catheterization via nursing-directed interventions and bundling of catheter care have been shown to decrease rates of CA-UTI.^{86,97,98}

Medical adjuncts and prophylaxis

Although there is some evidence that cranberry products and extracts decrease SUTIs in young women with recurrent UTIs, there is no clear evidence to recommend

the generalized use of cranberry extracts and products for prevention of CA-UTIs.⁹⁹ Likewise, methenamine salts may be considered for the reduction of CA-ASB and CA-UTI in patients after gynecologic surgery who have an indwelling urinary catheter for 1 week or less; however, methenamine salts should not be used routinely for patients with long-term intermittent or indwelling Foley catheters. If methenamine salts are used, the urinary pH should be 6.0 or less, but there are insufficient data to recommend how best to achieve that pH goal. Systemic antimicrobials should not be used for routine prophylaxis because of the increased risk for selecting out antimicrobialresistant organisms. Likewise, prophylactic antibiotics for either catheter placement or removal are not recommended for reduction of CA bacteriuria.

Catheter care

Reduction of urethral meatal colonization, a source for ascending bacterial infection, seems to be an excellent target for reduction of CA-UTIs. However, large randomized controlled trials do not support benefit to daily meatal cleaning with povidone-iodine solution, silver sulfadiazine, polyantibiotic ointment or cream, or soap and water. Irrigation of catheters with antimicrobial solutions may reduce CA-ASB in select patient populations, but its routine use is not recommended. There is insufficient evidence for routine catheter change in patients with functional long-term indwelling Foley catheters.

Summary: CA-UTIs

CA-UTIs are one of the most common health care-associated infections and can result in significant morbidity and prolongation of hospital stay. Critically ill patients tend to have a higher proportion of CA-ASB and CA-UTIs. It is important to recognize the indications for indwelling urinary catheters, and to remove them promptly once the indications are no longer valid. Proper catheter care and nursing bundles can reduce the incidence for CA-UTIs.

SSI

Epidemiology

SSI is a common infection in surgical patients, occurring in about 3% of all surgical procedures and in up to 20% of patients undergoing emergency intra-abdominal procedures. SICU patients can be particularly prone to this HAI. Severe skin and soft tissue infections, including those related to SSI, frequently require management in the ICU, in part related to associated septic shock or toxic shock syndrome or associated organ failure.¹⁰⁰ Beginning in 2012, hospitals participating in the CMS Inpatient Prospective Payment System will be required to report SSI data through NHSN, and these data will be included in the Inpatient Quality Reporting data, which are publicly reported by CMS at the Hospital Compare Web site.¹⁰¹

Risk Factors

SSI risk is strongly associated with wound classification, being low for the clean (class 1) and clean-contaminated (class 2, defined as gastrointestinal or genitourinary tract entered in a controlled manner) incisions and high for the contaminated (class 3, defined as open traumatic wounds, infected urine or bile, gross spillage from the gastrointestinal tract) and dirty-infected (class 4) incisions. Traditionally, SSI rates calculated by the CDC and NHSN have been risk-stratified using a risk index (NHSN Risk Index) of 3 equally weighted factors: the American Society of Anesthesiologists score, wound classification, and procedure duration.¹⁰² However, for some procedures, these variables are not associated with SSI risk, are not equally important in the risk they confer, and are candidates for replacement by other, more important

risk factor variables that should be taken into account. A set of new risk models was recently developed using existing data elements collected through NHSN, was associated with improved predictive performance, and will update the NHSN SSI risk index.¹⁰³ Laparoscopic surgery is associated with decreased SSI risk.

Diagnosis

SSI is categorized into superficial incisional, deep incisional, and organ/space SSI (intra-abdominal abscess or empyema, **Fig. 13**).¹⁰⁴ SSI rates should be followed for 30 days postoperatively, and for 1 year postoperatively in patients with implants.

Treatment

There are 4 fundamental management principles that are key to a successful outcome in caring for patients with severe skin infections, including SSI¹⁰⁵:

- 1. Early diagnosis and differentiation of necrotizing versus nonnecrotizing skin infection, including SSI
- 2. Early initiation of appropriate empiric broad-spectrum antimicrobial therapy, including anti-MRSA antibiotics, and consideration of risk factors for specific pathogens
- 3. Source control (ie, early aggressive surgical intervention for drainage of abscesses and debridement of necrotizing soft tissue infections)
- 4. Pathogen identification and appropriate de-escalation of antimicrobial therapy

Antimicrobial therapy is an essential element for skin infections. The choice of antimicrobial agent for empiric treatment of SSI should be guided by the site and type of infection, but in critically ill patients should include empiric parenteral anti-MRSA antimicrobial therapy.¹⁰⁶ Guidelines for the antimicrobial treatment of complicated skin

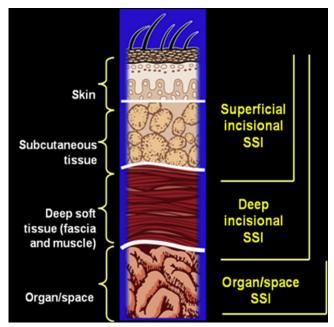


Fig. 13. SSI classification by the CDC.

infections provide comprehensive recommendations regarding antimicrobials.^{107,108} The most common causative pathogens in SSI are gram-positive pathogens, with *S aureus* as the most common SSI pathogen, with increasing rates of MRSA. In abdominal procedures, SSIs are caused roughly equally by gram-positive and gram-negative organisms. In transplant recipients, *Enterococci* are the most commonly isolated pathogens, and fungal SSIs are more common.

Prevention

The Surgical Care Improvement Project (SCIP) was created in 2003 as a collaborative effort to reduce morbidity and mortality in surgical patients. The SCIP-INF quality measures are focused on SSI prevention and listed below.

INF-1	Prophylactic antibiotics received within 1 hour before surgical incision (2 hours if receiving vancomycin)
INF-2	Prophylactic antibiotic selection: patient received appropriate recommended antibiotic for their specific surgical procedure
INF-3	Prophylactic antibiotics are discontinued within 24 hours after surgery end time (48 hours for cardiac surgery patients)
INF-4	Cardiac surgery patients with controlled 6 $_{AM}$ postoperative blood glucose level (\leq 200 mg/dL)
INF-6	Surgery patients with appropriate surgical site hair removal (clippers or depilatory or those not requiring surgical site hair removal)

Antimicrobial prophylaxis for SSI prevention is the most important component of the SCIP-INF measures. For an antibiotic to be effective prophylaxis for SSI, it should (1) cover the most likely pathogens that cause SSI for the particular procedure; (2) be administered such that tissue levels of antibiotic are sufficient to have antibiotic activity at the time of incision; and (3) carry minimal risk to the patient in terms of cost and side effects. SCIP provides a list of approved antibiotics for surgical procedures annually.

VTE

Epidemiology

VTE remains one of the most common preventable causes of in-hospital mortality. In the United States, approximately 600,000 cases of symptomatic VTE and 300,000 VTE-related deaths occur annually.¹⁰⁹ Two-thirds of these cases occur in hospitalized patients, and critically ill patients are at the highest risk for developing DVT or PE. The incidence of DVT can range from 28% to 32% in mixed medical-surgical ICU patients to as high as 60% in trauma patients or 70% in acute ischemic stroke patients.¹¹⁰

Risk Factors

The Virchow triad describes the 3 fundamental risks factors for development of VTE: venous stasis, endothelial injury, and hypercoagulable state. Clinical risk factors for VTE in ICU patients are common (**Table 5**).¹¹¹ We use the Caprini Risk Assessment Model as a tool to quantify an individual's risk for VTE, and guide decision making regarding the appropriate VTE prophylaxis regimen (**Fig. 14**).¹¹²

Diagnosis

SICU patients with suspected DVT should undergo venous duplex compression ultrasonography (CUS) of the 4 extremities as the best diagnostic test. D-dimer assay has

Table 5 ICU acquired risk factors for development of VTE	
General Medical Risk Factors	ICU Acquired Risk Factors
Advanced age	Immobilization
Malignancy	Stroke
Recent surgery	Trauma
Previous VTE	Mechanical ventilation
Pregnancy	Invasive procedures/tests
Obesity	CVCs
Oral contraceptives	Sepsis
Nephrotic syndrome	Heart failure
Inherited or acquired hemophilia	Vasopressor use
Inflammatory bowel disease	Cardiopulmonary failure

Data from Chan CM, Shorr AF. Venous thromboembolic disease in the intensive care unit. Semin Respir Crit Care Med 2010;31(1):39–46. PMID: 20101544.

a high sensitivity (98%) and modest specificity (50%), so is useful for excluding DVT but not useful for confirming diagnosis. It should not be used in surgical patients, pregnant women, or patients who have cancer. If CUS is positive, anticoagulation treatment should be initiated without performing any additional studies. However, if the initial CUS is negative, a follow-up CUS should be repeated at 1 week; 2 negative CUS scans rule out DVT (Fig. 15). In patients for whom CUS is not feasible or nondiagnostic, computed tomography (CT) venography or magnetic resonance venography may be useful for diagnosis. In the case of isolated distal DVT, serial testing is recommended to rule out proximal extension. Patients who have suspected recurrence of DVT on the ipsilateral extremity should undergo CUS as an initial diagnostic modality; however, if the CUS is abnormal but nondiagnostic, further evaluation should be performed with venography. Pregnant patients with symptoms of DVT should be evaluated with CUS, followed by duplex ultrasonography of the iliac vein if CUS is negative.¹¹³ Patients with suspicion for upper extremity DVT should be initially evaluated with Doppler CUS. If clinical suspicion is high, but initial ultrasonography is negative for DVT, further evaluation with moderate or highly sensitive D-dimer, serial ultrasonography, or venography is necessary. In ICU patients with possible PE, CT pulmonary angiography is indicated.

Treatment

Choice of therapy

Patients diagnosed with acute proximal DVT should be initiated on parenteral anticoagulation therapy; options are low-molecular-weight heparin (LMWH), fondaparinux, intravenous unfractionated heparin (IV-UFH). If the clinical suspicion is high, or if there is a delay of more than 4 hours to obtaining diagnostic test results, it is recommended that anticoagulation therapy be initiated empirically; however, if the clinical index of suspicion is low, then anticoagulation therapy should be withheld until diagnostic test results are available. Isolated DVT of the distal lower extremity veins generally does not require anticoagulation therapy unless there is development of extension on follow-up CUS (over 2 weeks) or if the patient has severe symptoms or risk factors for clot extension.¹¹⁴

Dosing

LMWH or fondaparinux is preferred over IV-UFH and subcutaneous (SC) UFH. In acute episodes of VTEs, treatment with once-daily dosing of LMWH is preferred

Prophylaxis Orders (For use in Elective General Surgery Patients) Thrombosis Risk Factor Assessment (Choose all that apply) Image: State of the state of		Deep Vei	n Thromb	osis (DVT)		BIRTHDATE
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VTE Prophylaxis Contraindicated, Reason:	5 or more	Highest Risk	40-80%	Choose <u>QNE of the following madications PLUS</u> compression devices: □ Hegarinal Compression Device (SCD) □ Hegarin 5000 units SQ TID (Preferred with Epidurals) □ Enoxaparin/Lovenox (Preferred): □ 40mg SQ daily (WT < 150kg, CrCl > 30mL/min) □ 30mg SQ daily (WT < 150kg, CrCl = 10-29mL/min) □ 30mg SQ BID (WT > 150kg, CrCl > 30mL/min)		
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Fig. 14. Caprini VTE risk assessment tool to determine appropriate VTE prophylaxis. University of Michigan DVT prophylaxis orders using the Caprini Risk Assessment Model to guide (1) patient risk stratification for development of VTE, and (2) selection of appropriate DVT prophylaxis regimen.

over twice-daily dosing. Local considerations such as cost, availability, and familiarity of use dictate the choice between fondaparinux and LMWH. Patients placed on IV-UFH should have an initial bolus of 80 units/kg followed by initial drip rate at 18 units/kg/h (bolus 70 units/kg followed by 15 units/kg/h for cardiac or stroke patients); alternatively patients may be placed on fixed initial bolus dose of 5000 units followed by 1000 units/h. Patients with renal insufficiency (creatinine clearance <20 mL/min) should receive reduced doses of LMWH. Conversely, in morbidly obese patients with VTE and weight greater than 100 kg, fondaparinux dosing should be increased

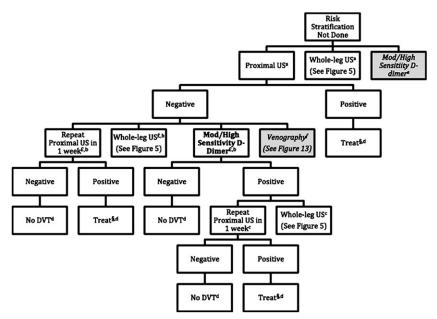


Fig. 15. Recommendations for evaluation of suspected first lower extremity DVT: risk stratification not performed. (*From* Bates SM, Jaeschke R, Stevens SM, et al. American College of Chest Physicians. Diagnosis of DVT: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(Suppl 2):e395S; with permission.)

from the usual dose of 7.5 mg to 10 mg daily. In the absence of a need for rapid anticoagulation reversal, vitamin K antagonist (VKA) therapy, such as warfarin, should be started on day 1 or 2 of parenteral anticoagulation therapy. Parenteral anticoagulation should be continued for a minimum of 5 days and the international normalized ratio INR is 2.0 or more. The goal therapeutic range is an INR of 2.0 to 3.0 (target INR of 2.5). In patients who have an acute proximal DVT of the leg but have contraindications to anticoagulation, placement of an inferior venal cava filter is recommended, with subsequent initiation of anticoagulation once bleeding risk is resolved.¹¹⁵

Duration

Patients with a first episode of VTE (DVT or PE) should be treated for 3 months. If the VTE was unprovoked (ie, no risk factors), continuation of therapy may be reassessed after 3 months. Patients with recurrent VTE and who have a low bleeding risk should undergo extended anticoagulation therapy. VKAs are recommended in most patients with DVT; however, patients with VTE and cancer should be treated with LMWH. Compression stockings are recommended as adjunct treatment of patients with acute DVT.¹¹⁶

PE

In patients who have PEs without associated hypotension, the treatment algorithm is similar to DVT treatment. However, patients who have PE with associated hypotension should undergo (in order of preference) thrombolytic therapy, catheter-assisted thrombolectomy, or surgical pulmonary embolectomy.

Table 6 VTE prophylaxis option for surgice	al patients
Surgery Type	Recommended Prophylaxis Options ^a
Intracranial neurosurgery	Any of the following: IPC devices with or without GCS LD-UFH LMWH ^b LD-UFH or LMWH ^b combined with IPC or GCS
General surgery	Any of the following: LD-UFH LMWH Factor Xa inhibitor (fondaparinux) LD-UFH or LMWH or factor Xa inhibitor (fondaparinux) combined with IPC or GCS
General surgery with a reason for not administering pharmacologic prophylaxis	Any of the following: GCS IPC devices
Gynecologic surgery	Any of the following: LD-UFH LMWH Factor Xa inhibitor (fondaparinux) IPC devices LD-UFH or LMWH or factor Xa inhibitor (fondaparinux) combined with IPC or GCS
Urologic surgery	Any of the following: LD-UFH LMWH Factor Xa inhibitor (fondaparinux) IPC devices GCS LD-UFH or LMWH or factor Xa inhibitor (fondaparinux) combined with IPC or GCS
Elective total hip replacement	Any of the following started within 24 h of surgery: LMWH Factor Xa inhibitor (fondaparinux) Warfarin
Elective total knee replacement	Any of die following: LMWH Factor Xa inhibitor (fondaparinux) Warfarin IPC devices VFP
Hip fracture surgery	Any of the following: LD-UFH LMWH Factor Xa inhibitor (fondaparinux) Warfarin
Elective total hip replacement with a reason for not administering pharmacologic prophylaxis	Any of the following: IPC devices VFP (continued on next page)

(continued)	
Surgery Type	Recommended Prophylaxis Options ^a
Hip fracture surgery with	Any of the following:
a reason for not	GCS
administering	IPC devices
pharmacologic prophylaxis	VFP

Abbreviations: GCS, graduated compression stockings; VFP, venous foot pump.

^a Patients who receive neuraxial anesthesia or have a documented reason for not administering pharmacologic prophylaxis may pass the performance measure if either appropriate pharmacologic or mechanical prophylaxis is ordered.

Current guidelines recommend postoperative LMWH for intracranial neurosurgery.

Upper extremity DVT

In general, upper extremity DVTs are treated in the same manner as lower extremity DVTs. The development of a UE DVT associated with CVCs does not mandate catheter removal if it is still functional and there is an ongoing need for central venous access. If the catheter remains indwelling for longer than 3 months, then anticoagulation therapy should be extended.

Table 7 Recommendations for thromboprophylaxis in various risk groups						
	Risk and Consequences of Major Bleeding Complications					
Risk of Symptomatic VTE	Average Risk (~1%)	High Risk (~2%) or Severe Consequences				
Very low (<0.5%)	No specific prophylaxis					
Low (~1.5%)	Mechanical prophylaxis, preferably v	with IPC				
Moderate (~3.0%)	LD-UFH, LMWH, or mechanical prophylaxis, with IPC	Mechanical prophylaxis, preferably with IPC				
High (~6.0%)	LD-UFH or LMWH plus mechanical prophylaxis with ES or IPC	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added				
High-risk cancer surgery	LD-UFH or LMWH plus mechanical prophylaxis with ES or IPC and extended-duration prophylaxis with LMWH after discharge	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added				
High risk, LDUH and LMWH contraindicated or not available	Fondaparinux or low-dose aspirin (160 mg); mechanical prophylaxis, preferably with IPC; or both	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added				

See Table 5 for details about risk stratification for VTE.

Abbreviation: ES, elastic stockings.

Data from Gould MK, Garcia DA, Wren SM, et al; American College of Chest Physicians. Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(Suppl 2):e2275–775. PMID: 22315263.

Special considerations

Patients with symptomatic thrombosis of hepatic or splanchnic veins (eg, portal, mesenteric, or splenic veins) should be treated with anticoagulation; however, asymptomatic patients should not be treated.

Reversal of Anticoagulation

In patients who require cessation of anticoagulation for anticipated major surgery or interventional procedure, VKAs should be stopped 5 days before surgery, and resumption of VKAs 12 to 24 hours after procedure and adequate hemostasis. Patients with mechanical heart valve, atrial fibrillation, or VTE at high risk for a thromboembolic event, bridging anticoagulation with a parenteral agent is advised; low-risk patients do not require bridging anticoagulation therapy. Patients who are on therapeutic SC-LMWH should have their anticoagulation stopped 24 hours before major surgery/intervention. Patients undergoing surgery with a high risk of bleeding should not resume anticoagulation therapy until 48 to 72 hours postoperatively.¹¹⁷ In patients who are on VKAs and have an acute bleeding episode requiring reversal, 4-factor prothrombin complex concentrate (PCC) is the recommended treatment. In addition, patients should receive slow IV injection of vitamin K 5 to 10 mg.

Prevention

Patients who are critically ill are at high risk for development of VTE. ICU patients should receive pharmacologic thromboprophylaxis (either LMWH or low-dose UFH [LD-YFH]) in addition to mechanical prophylaxis with intermittent pneumatic compression (IPC) devices. Perioperative prophylaxis options for patients undergoing surgery are summarized in **Table 6**. In patients with high bleeding risk, mechanical prophylaxis with IPC is sufficient until bleeding risk decreases, at which point they should also receive chemoprophylaxis (**Table 7**).

Summary: VTE

VTE is a source of major morbidity and mortality in hospitalized patients. Critically ill patients represent a population who are at increased risk for VTE and should receive appropriate VTE prophylaxis. Routine screening for DVT is not recommended. However, in patients for whom there is a high index of suspicion, duplex CUS is a good screening modality. Treatment should be initiated for proximal VTE events, initially with parenteral anticoagulation; VKAs should be used once the patient no longer has bleeding risk. PCC is the recommended treatment of VKA-related bleeding.

SUMMARY

Critically ill patients in ICUs are subject to many complications associated with the advanced therapy required for treatment of their serious illnesses. Many of these complications are HAIs and are related to indwelling devices. These complications include VAP, CLABSI, and CA-UTI. SSI is also a common complication amongst SICU patients. VTE, including DVT and PE, is another common complication in critically ill patients. All efforts should be undertaken to prevent these complications in surgical critical care, and national efforts are under way for each of these complications.

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