Common complications in the surgical intensive care unit

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Surgical and trauma intensive care units provide the facilities, resources, and personnel needed to care for patients who have been severely injured, present with acute surgical emergencies, require prolonged and complex elective surgical procedures, or have severe underlying medical conditions. Correcting the immediately evident physiologic derangement is only the first step in the care of these patients, because in many cases their prognosis and ultimate outcome will depend on whether additional insults accrued during their intensive care unit and hospital stay will prevent them from a full recovery. The nature, number, and complexity of the interventions used to provide advanced support requires a unique attention to the concept of patient safety, particularly when the population involved is that most vulnerable to injury and with the least amount of physiologic reserve to recover from it. The medical community, the public, and even regulatory agencies have focused on specific preventable complications that are common in surgical and injured patients, such as medical errors, healthcare-associated infections, and venous thromboembolism. Enough scientific knowledge has been obtained through well-conducted clinical trials to generate detailed evidence-based guidelines for the prevention and management of some of these pathologies, but still there are outstanding questions in terms of the applicability of the recommendations to the critically ill. In addition to clinical and technical expertise, performance improvement and quality monitoring activities provide direction for system solutions required to properly address many complications that are not provider specific. (Crit Care Med 2010; 38[Suppl.]:S483–S493)

KEY WORDS: intensive care units; cross infection; pneumonia; ventilator-associated; catheter-related infections; pulmonary embolism; venous thromboembolism; postoperative complications; medical errors; critical care; quality assurance; health care

With the growth in volume and complexity of the surgical procedures performed in the United States and the development of a comprehensive trauma system, we have learned that the final outcome of our critically ill surgical and trauma patients depends, to a large extent, on events that take place after the original injury, surgical emergency, or elective procedure. These events occur under our watch, as a result of our action or inaction, and are determined by our medical knowledge, technical skills, and the systems and technology that we use in our intensive care units (ICUs). If we remember that 2,400,000 patients are admitted to >6,000 ICUs each year in the United States, and 200,000 die in the ICU, we can get a better idea of the potential impact of interventions designed to prevent or mitigate the effect of complications during their ICU stay (1, 2).

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Although surgical ICUs may not be as costly or have as many deaths as medical ICUs because of differences in underlying chronic pathology and demographics, surgical and trauma patients invariably have experienced a sudden and profound systemic insult that may lead to decompensation of subclinical conditions and set the stage for new and potentially life-threatening complications. They need aggressive diagnostic and therapeutic interventions and might also experience operative complications, missed injuries, and secondary injuries, to name a few (3).

Because we have recognized the repercussions of complications in the ICU in terms of mortality, morbidity, and cost burden to the institution, performance improvement activities have become part of the comprehensive care of surgical patients. Deaths and complications are evaluated in terms of preventability and provider specificity, allowing identification for opportunities to improve (4–6). Focusing on the differences between trauma and surgical patients, for example, Frankel et al (7) studied preventable adverse events in their surgical ICU patients and found they were rarely provider specific; therefore; they concluded that system solutions and changes in pre-ICU care would be most beneficial, rather than other efforts directed at the provider. A summary of their findings in >1,000 complications over a 3-yr period is illustrated in Figure 1.

When we accept the challenge of taking care of critically ill surgical patients, we understand that in many cases we will witness a worsening clinical condition. In some cases, this scenario reflects the progression of the underlying disease process: an overwhelmed host unable to maintain the integrity of his organs, despite our best efforts. In other cases, he or she might be a victim of unnecessary interventions, omissions, or medical errors. The purpose of this chapter is to present a thorough review of available evidence on interventions that might enable us to decrease the number of patients in the latter group, and provide compassionate and appropriate care to those on the former. There is a significant amount of literature that suggests that this is an attainable goal, resulting in considerably better outcomes (8, 9). We will start by presenting the concept of safety in the ICU; next, we will explore the topic of healthcare-associated infections with emphasis on pneumonia and catheter-related bloodstream infections; and we will conclude by reviewing venous thromboembolism.

Patient Safety

Since the first official use of the term *patient safety* in 1984 by the American

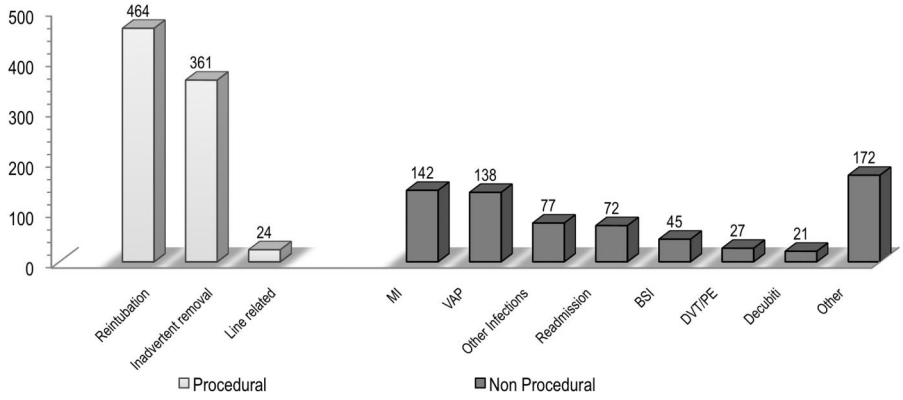

Figure 1. Distribution of 1158 complications in a surgical intensive care unit over 3 yrs. *MI*, myocardial infarction; *VAP*, ventilator-associated pneumonia; *BSI*, bloodstream infection; *DVT*, deep vein thrombosis; *PE*, pulmonary embolism. Data with permission from Frankel et al (7).

Society of Anesthesiologists, we have witnessed increased awareness both by the healthcare community, and the public, regarding the significant risk associated with the delivery of care, even in the best institutions. In 1999, the Institute of Medicine of the National Academy of Sciences released the report, "To Err Is Human: Building a Safer Health System," calling for a national effort to identify, report, and prevent adverse events. This report received wide publicity, particularly the worrisome estimate of 44,000–98,000 preventable deaths annually due to medical errors. Today, the concept of patient safety has grown to the point of being considered a "new healthcare discipline" (10), and we have learned many valuable lessons, as a result of numerous clinical trials and initiatives in terms of monitoring, prevention, and early safety interventions.

Caring for surgical and trauma patients only raises the bar in terms of patient safety, because we have to take into account secondary injuries, missed injuries, and procedural complications; all of these in patients, for the most part, were fully ambulatory and with good functional status before their accident or elective procedure. Although complications occur at a relatively consistent rate, any adverse drug event, new infection, or other complication is generally perceived as unfair and unexpected.

In the ICU, the magnitude of the physiologic derangement, the complexity and number of simultaneous interventions, the number of providers with different levels of training and expertise, and the technology involved in the care of our patients means that, in some cases, a real difference in the outcomes will depend on variables, such as time commitment of the medical staff, nurse/patient ratio, standardized care of catheters and tubes, efficient communication pathways, and computerized order entry systems, instead of new diagnostic and therapeutic interventions (11). In this context, a number of large-scale private, academic, and government initiatives to monitor and improve the quality of intensive care delivery are taking place, with special emphasis on patient safety and prevention of complications (2, 12).

Healthcare-associated Infections

During 2002 in the United States, 24% of 1.7 million estimated healthcare-associated infections (HAIs) took place in ICUs, with a rate of 13 per 1,000 patient-days. Analysis of data from hospitals participating in the U.S. National Nosocomial Infections Surveillance (NNIS) system indicates that, among 155,668 deaths, 98,987 were caused by or associated with HAIs, including almost 36,000 for pneumonia, 30,000 for catheter-related bloodstream infections, 13,000 for urinary tract infections, and 8,000 for surgical site infections (13).

HAIs can also lead to functional disability, emotional distress, increased ICU and hospital stay, and possible other long-term sequelae with reduced quality of life. When we consider the cost associated with each HAI episode and the prevalence of this entity, it becomes clear that HAIs constitute a significant burden for the whole healthcare system. There are marked differences in rates of HAIs between nations and from institution to institution; this fact, along with the favorable response to carefully planned and coordinated initiatives, indicates that a good number of these infections are avoidable. The rate of HAIs is an outcome measure used as an indicator of the quality of care provided in many institutions, to the point that several states have enacted legislation that requires mandatory disclosure of rates of HAIs (14).

Clear definitions and precise terminology have become essential in terms of treatment decisions, epidemiologic surveillance, reporting, etc. The U.S. Centers for Disease Control and Prevention (CDC) and National Healthcare Safety Network (formerly NNIS) have published the current definitions and diagnostic criteria accepted nationally, by the International Nosocomial Infection Control Consortium, and several other institutions throughout the globe.

Healthcare-associated infection or HAI (instead of "nosocomial") is defined as a localized or systemic condition, resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s). There must be no evidence that the infection was present or incubating at the time of admission to the acute care setting (15–17).

Risk factors and prevention

Hospital-acquired infections are significantly different from community-acquired infections, and they occur in the setting of multiple-enabling conditions and circumstances that have been found to correlate with the development of infection and eventual outcome. These factors can be summarized by focusing on the host, the pathogen, and the environment.

Host defense mechanisms that are compromised in trauma and surgical ICU patients include the skin and mucosal integrity, cellular and humoral immunity due to poor nutritional status or immunosuppressive medications, preexisting medical conditions like diabetes, and the presence of indwelling devices susceptible to bacterial colonization. Correction of some of these factors like strict glycemic control in surgical, cardiac, and trauma units (18–20) has been found to be more important than previously realized and is the focus on active research with promising results. Medical devices are so closely associated with HAIs that multiple publications and texts refer to the whole subject as "device-related infections." The list of devices named in recent studies continues to grow, including ventilators, central venous catheters, surgical drains, urinary catheters, gastrointestinal catheters, heart valves, ventricular as-

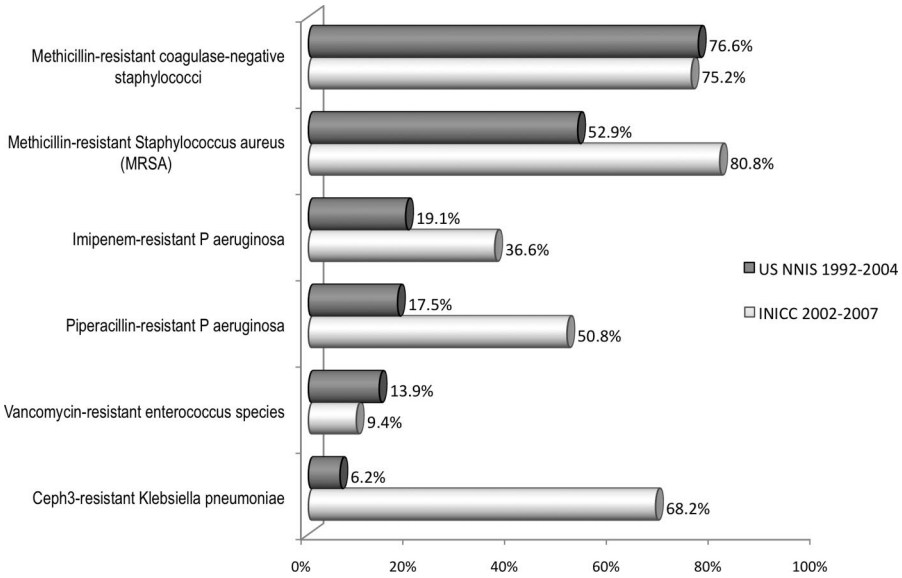

Figure 2. Comparison of antimicrobial resistance rates in the intensive care units of the U.S. National Nosocomial Infections Surveillance System (*NNIS*) and the International Nosocomial Infection Control Consortium (*INICC*). *Ceph3*, third-generation cephalosporins. Data with permission from Rosenthal et al (23).

sist devices, coronary stents, neurosurgical ventricular shunts, implantable neurologic stimulators, arthroprostheses, fracture-fixation devices, inflatable penile implants, breast implants, cochlear implants, intraocular lenses, and dental implants (21).

The pathogens identified in ICU patients have demonstrated a rapid incease in the rate of resistance to antimicrobial agents worldwide, with increasing number of isolates of vancomycin-resistant enterococci, methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa* resistant to imipenem, and others, as noted in Figure 2 with data from the U.S. NNIS system and the International Nosocomial Infection Control Consortium (22–24).

The likelihood of recovering multidrug resistant (MDR) pathogens increases after receiving antimicrobial therapy due to selective pressure. A good example is the emergence of piperacillin resistant *P. aeruginosa* in patients receiving fluoroquinolones (25, 26). Considering that the presence of resistant pathogens is associated with adverse outcomes, including increased mortality (27, 28), effective antimicrobial stewardship and a comprehensive infection control program are a necessity in modern ICU care (29).

The hospital or healthcare environment is where the interaction between the susceptible host and a number of pathogens takes place. It is the common denominator in our definition of HAIs and has become the focal point of a number of preventive interventions, some of which have proven to be extremely successful and cost-effective, when dealing with these infections. The patient rooms may harbor significant pathogens even after the source patient has moved (30). Water and air filtration systems have also been colonized by fungi and bacteria (31, 32). The healthcare worker is one of the most important vectors within this environment, and his or her compliance with the current recommendations regarding hand hygiene, isolation protocols, and others will impact the rate of HAIs (33).

Hospital-acquired Pneumonia and Ventilator-associated Pneumonia

Hospital-acquired pneumonia (HAP) is defined as an inflammatory condition of the lung parenchyma caused by infectious agents not present or incubating at the time of admission. Ventilator-associated pneumonia (VAP) is a subset of HAP and refers to pneumonia that arises >48–72 hrs after endotracheal intubation. VAP occurs almost exclusively in the ICU and represents >85% of ICU HAP (34, 35).

Epidemiology

HAP is the second most common HAI in the United States and has been clearly associated with elevated morbidity and mortality. The NNIS System of the CDC reported that between 2006 and 2008, the rate of VAP in the United States per 1,000 ventilator-days was 2.4 for medical ICUs, 4.9 for surgical ICUs, 8.1 for trauma units, and 10.7 for burn units (24). The NNIS annual reports (22, 36) showed that these rates have been declining consistently by approximately 50% during the last decade. VAP is associated with increases in the length of ICU stay, hospital stay, and ventilator-days, with costs that have been estimated between $10,000 and $40,000 per event (37–39). Patients with VAP have mortality rates that range from 20% to >70% in specific populations, depending on the infecting organism. Multiple matched cohort studies designed with the purpose of quantifying the mortality directly attributable to the VAP, however, have produced conflicting results. At least four studies have failed to demonstrate any statistically significant difference in mortality between VAP cases and carefully matched controls without pneumonia (37, 38, 40, 41); four additional studies (42–45) have reported excess mortality from 15% to 50% in cases compared with the controls. Although these studies do not agree in terms of diagnostic and matching criteria, a meta-analysis by Safdar et al (46) has attempted to pool the results: the summary estimate (odds ratio) for ICU mortality in six studies in which it was reported was 2.03 (95% confidence interval, 1.16–3.56, p = .05); however, significant statistical heterogeneity was found. Pooled results from the four studies that evaluated mortality during the entire duration of hospitalization yielded an odds ratio of 1.64 (95% confidence interval, 0.86–3.14).

Risk factors

Risk factors for the development of HAP can be differentiated into modifiable and nonmodifiable and into patient-related or treatment-related. Nonmodifiable patient-related risk factors include male sex, preexisting pulmonary, cardiac, or neurologic disease, coma, acquired immune deficiency syndrome, head trauma, and multiple organ failure. Nonmodifiable treatment-related factors include neurosurgery, thoracic surgery, and intrahospital transportation.

Modifiable risk factors identified in retrospective studies are the natural target for intervention. It is important to emphasize that causality is very difficult to demonstrate with observational studies, yet some

Table 1. Evidence-based guidelines and recommendations from the U.S. Centers for Disease Control, the American Thoracic Society, and the Infectious Diseases Society of America, for the prevention of healthcare-associated pneumonia (34, 35)

Infection Control
Hand hygiene
Contact precautions
Microbiological surveillance
Intubation and Invasive Devices
Consider noninvasive ventilation
Avoid reintubation
Oral intubation instead of nasotracheal
Cuff pressure >20 cm H_2O
Limit sedatives and paralytic agents, and use daily interruption
Continuous aspiration of subglottic secretions
Avoid flushing the condensate into the lower airway
Circuit changes not more than once a week, except if visibly soiled
Use a heat and moisture exchanger with a bacterial filter
Closed suctioning catheters should be used
Aspiration, Body Position, and Enteral Feeding
Semirecumbent positioning particularly during feeding (30° to 45° angle)
Enteral nutrition is preferred over parenteral nutrition
Kinetic beds in selected patients
Antimicrobial Modulation of Host Bacterial Colonization
Oral antiseptic to reduce oropharyngeal colonization
Oral or systemic antibiotics not routinely recommended for prevention
Stress Bleeding Prophylaxis, Transfusion, and Hyperglycemia
Use prophylaxis with H_2 antagonist, sucralfate, or proton pump inhibitor
Restrict transfusions, consider leukocyte-depleted units
Strict glucose control

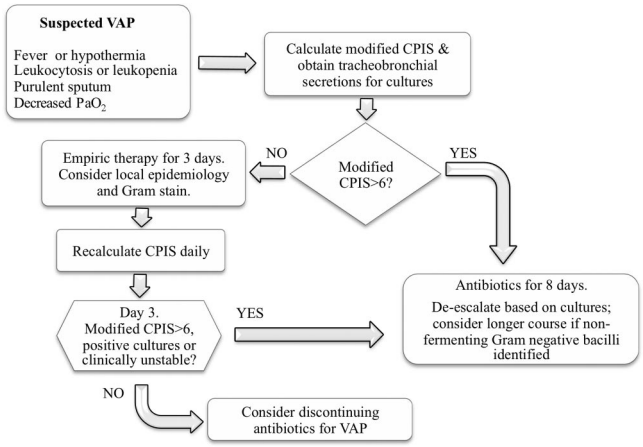

Figure 3. Diagnosis and antibiotic management of ventilator associated-pneumonia (*VAP*) in the surgical intensive care unit. *CPIS*, Clinical Pulmonary Infection Score. Adapted with permission from Leong and Huang (48).

of the most prominent modifiable factors are: duration of mechanical ventilation, patient positioning, stress ulcer prophylaxis, enteral nutrition, use of paralytic agents, transfusions, glucose control, antibiotics, and antiseptics (47, 48).

Prevention

Effective prevention strategies supported by well-conducted, randomized, clinical trials (level I), controlled nonrandomized trials, or large series of cases (level II) include general prophylaxis and infection control, microbiological surveillance with availability of data on local drug-resistant pathogens, programs to reduce or alter antibiotic prescribing practices, and a number of interventions that have been used by the CDC, the Infectious Diseases Society of America, and the American Thoracic Society in the preparation of comprehensive evidence-based guidelines for the prevention of HAP as summarized in Table 1 (34, 35, 49).

In an effort to consistently improve the quality of care provided in ICUs nationwide, particularly regarding mechanical ventilation and complications like VAP, the Institute for Healthcare Improvement has proposed the concept of "bundles," in this case, the ventilator bundle, as a tool that will allow clinicians and administrators to focus their efforts in a limited number of carefully selected evidence-based interventions. The ventilator bundle includes:

- Elevation of the head of the bed
- Daily sedation interruption
- Peptic ulcer disease prophylaxis
- Deep vein thrombosis prophylaxis

The adherence to the ventilator bundle has resulted in decreased rates of VAP in ICUs around the country. It is interesting that, even though the different elements of the bundle have been associated with ICU outcomes, only the first two have been shown to decrease the rate of VAP; peptic ulcer prophylaxis might increase the risk. It has been argued that grouping care processes together into simple bundles, in an "all or none" application as an indicator of quality, requires multiple elements of the ICU to organize their work, resulting in better outcomes (50, 51).

Diagnosis

HAP and VAP present an important clinical challenge because there is no diagnostic gold standard and both underdiagnosis and overdiagnosis might lead to undesired outcomes. We can start by defining what the optimal diagnostic algorithm should enable us to do: accurate identification of patients with pulmonary infection, timely collection of cultures, early initiation of appropriate antibiotics at the same time allowing de-escalation of therapy, and identification of patients with extrapulmonary sources of infection (48).

Currently, a combination of clinical and microbiological strategies for the diagnosis of VAP provide the best opportunity to achieve these desired goals. Figure 3 demonstrates the different elements of the algorithm.

The clinical approach defines the presence of HAP by new lung infiltrates plus at least two of three clinical features: fever of >38°C, leukocytosis or leukopenia, and purulent secretions. Clinical suspicion is followed by the collection of sputum samples or endotracheal aspirates for microscopic examination and cultures. The Clinical Pulmonary Infection Score (CPIS) has emerged as a useful tool in the assessment of patients with suspected VAP. It was originally developed by Pugin and co-workers (52) to compare the ability of sampling techniques to differentiate pneumonia from colonization, and in that setting a good correlation of a CPIS >6 with the presence of pneumonia (defined by quantitative cultures) was found. Subsequent validation studies, using microbiological criteria, histology, and postmortem cultures as the gold standard, showed relatively low sensitivity and specificity, limiting the utility of the CPIS alone as a diagnostic tool. More

Table 2. Modified Clinical Pulmonary Infection Score (CPIS)

Diagnostic Feature	CPIS Range	CPIS Score
Temperature (°C)	36.5–38.4	0
	38.5–39.0	1
	<36.0 or >39.0	2
White blood cells ($\times 10^9$/L)	4.0–11	0
	11–17	1
	>17	2
Secretions	Rare	0
	Abundant	1
	Abundant and purulent	2
Pao_2/Fio_2 (torr)	>240 or ARDS	0
	≤240 no ARDS	2
Chest radiograph infiltrates	None	0
	Diffuse or patchy	1
	Localized	2
Progression of pulmonary infiltrate	No radiographic progression	0
	Radiographic progression (CHF and ARDS excluded)	2
Microbiology	Negative	0
	Positive cultures	1
	Positive plus positive Gram-negative stain	2

CHF, congestive heart failure; ARDS, acute respiratory distress syndrome.

CPIS score originally published by Pugin et al (52). Modified for clinical use according to Singh et al (53).

Table 3. Wells' clinical probability score (91)

Variables	Points
Clinical signs and symptoms of DVT	3.0
An alternative diagnosis is less likely than PE	3.0
Heart rate >100	1.5
Immobilization or surgery in the previous 4 wks	1.5
Previous DVT/PE	1.5
Hemoptysis	1.0
Malignancy	1.0

DVT, deep venous thrombosis; PE, pulmonary embolism.

Based on Wells et al (91) with permission from Schattauer GmbH.

recently, Singh and co-workers (53) have modified the CPIS for clinical use, specifically for screening, initiation and length of antibiotic use, with good results. The modified version of the CPIS appears as part of the algorithm for diagnosis and initial therapeutic approach in patients with HAP/VAP in the guidelines published by the AmericanThoracic Society/Infectious Diseases Society of America in the United States and the Association of Medical Microbiology and Infectious Disease in Canada (34, 49).

The bacteriologic strategy relies on quantitative cultures of lower respiratory secretions, either endotracheal aspirates, bronchoalveolar lavage, or protected specimen brush samples to diagnose HAP/VAP and to determine the causative microorganism(s) (55, 56). The choice of method, the criteria for positivity, and the role of these results within the therapeutic decision tree depend on the local expertise and resources.

Treatment

Each institution should develop customized guidelines and recommendations in terms of antibiotic use based on local isolates and susceptibility profiles. The initial choice of antibiotic should include a careful evaluation of the risk factors for MDR pathogens like antimicrobial therapy or hospitalization in the preceding 90 days, current hospitalization >5 days, residence in nursing home or extended care facility, home infusion therapy or wound care, chronic dialysis, high frequency of antibiotic resistance in the community or hospital unit, family member with MDR pathogen, immunosuppressive disease or therapy (34).

A clinically stable patient with early-onset pneumonia and no risk factors can be treated with limited spectrum therapy, to be chosen based on the Gram-negative stain. Ceftriaxone, ampicillin/sulbactam, ertapenem, or a fluoroquinolone are all good options.

Late-onset or the presence of MDR risk factors indicate the use of broad-spectrum coverage, potentially including an antipseudomonal cephalosporin, penicillin, carbapenem or fluoroquinolone, and also vancomycin or linezolid to cover Gram-positive microorganisms, including methicillin-resistant *Staphylococcus aureus*.

If serial assessment shows adequate response to therapy, then de-escalation should follow, and a course of 8 days of antimicrobials would be appropriate, with the possible exception of patients with nonfermenting Gram-negative bacilli (i.e., *P. aeruginosa*, *Acinetobacter* species, or *Stenotrophomonas*); for these organisms, a longer duration of therapy has been associated with less recurrence although no difference in eventual mortality. A patient who does not respond should be evaluated for a noninfectious pulmonary diagnosis, extrapulmonary infections, or other complications.

Catheter-related Bloodstream Infections

Bloodstream infections (BSI) are an important focus on epidemiologic surveillance, considering an estimate >250,000 cases every year in the United States, 80,000 of which occur in ICU patients who have central venous catheters in place and are reported as central line (catheter)-associated BSI (CLABSI) (24, 57).

The guidelines published by the CDC in 2002 and by the Infectious Diseases Society of America in 2009 emphasize the surveillance definition of catheter-associated BSI for the purpose of screening and reporting, recognizing that it would overestimate the true incidence of clinically relevant catheter-related BSI (CRBSI) (57, 58).

The surveillance definition of BSI requires positive blood cultures, with or without signs of inflammatory response (according to the isolated microorganism), and no evidence of other source of infection. In some circumstances, a strong clinical suspicion with subsequent treatment for sepsis will be enough to configure the diagnosis of BSI even without positive cultures, particularly in the pediatric population. In a patient with systemic evidence of sepsis and no other source, an infection would be considered a CLABSI if a central catheter was used during the 48-hr period before its development even with negative blood cultures (15, 57).

Clinical definitions look for objective evidence that would allow the identification of the catheter as the source of the BSI like positive semiquantitative (>15 colony-forming units/catheter segment) or quantitative ($>10^3$ colony-forming units/catheter segment) cultures of the

catheter itself; differential time to positivity (>2 hrs) or elevated ratio (≥5:1 quantitative) when comparing samples obtained from the catheter and a peripheral vein; local inflammation or suppuration at the exit site, the tunnel, or subcutaneous pocket, or growth of the same organism from the infusate.

Epidemiology and pathogenesis

The National Healthcare Safety Network of the CDC reported that between 2006 and 2008, the rate of laboratory confirmed CLABSI per 1000 central catheter-days was 2.0 for medical ICUs, 2.3 for surgical ICUs, 3.6 for trauma units, and 5.5 for burn units. During this period, the central catheter utilization ratio for these units was 0.5 to 0.6 (central catheter-days/patient-days) (24).

Outcome studies have shown that the presence of CLABSI is clearly associated with prolonged length of stay and increased costs. Crude mortality rates have been estimated around 30%, but it has been difficult to obtain a clear answer about attributable mortality. Adjusting for severity of illness before the onset of the BSI has shown in several matched cohort studies results ranging from no difference in mortality to a 25% attributable mortality with a three-fold increase in risk of death (59–64).

Regarding the pathophysiology of CLABSI, the presence of the catheter gives the microorganisms access to the bloodstream by three pathways:

1. Skin organisms present at the insertion site can migrate into the cutaneous tract with colonization of the catheter tip (65).
2. Contamination of the hub when the catheter is accessed for blood draws or administration of medications allows intraluminal colonization. This is frequently the route in long-term catheters (66).
3. Hematogenous seeding (57).

Using the nationwide SCOPE database, 24,179 cases of hospital-acquired BSI in 49 institutions were analyzed by Wisplinghoff et al (67), finding that the most frequently isolated organisms were staphylococci and *Candida* (Fig. 4). They were able to identify an increase in the proportion of BSI caused by multiresistant organisms.

It is notable that, before the 1980s, the leading group of pathogens isolated from patients with BSI were Gram-negative bacilli, but more recently Gram-positive aerobes and *Candida* species have increased in frequency, possibly due to selection pressure and enhanced identification and recognition (68).

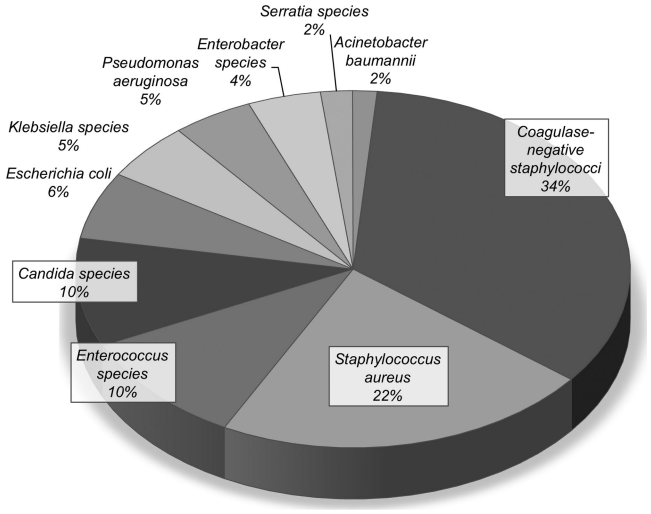

Figure 4. Distribution of the pathogens most commonly isolated from monomicrobial hospital-acquired bloodstream infections. Data with permission from Wisplinghoff et al (67).

Prevention

Given that catheter-associated BSI are caused by our interventions, it becomes clear that the best approach to decrease or eliminate the morbidity and possible mortality related to BSI is prevention. Accordingly, a great deal of data has been produced in reference to interventions designed to decrease the incidence of these infections, and several reviews and official guidelines (57, 69) have been published summarizing these studies. The most important measures are strict adherence to hand hygiene and the use of strict aseptic techniques during insertion, dressing changes, and manipulation of the catheter. Other important considerations include a careful decision about site of catheter insertion (subclavian, if possible), type of catheter (tunneled or cuffed, limit number of lumens), catheter material (Teflon or polyurethane), catheter coating with heparin, impregnation with antimicrobials or antiseptics, site dressings (chlorhexidine impregnated sponge), and prompt removal of catheter as soon as it is no longer needed. Additional interventions that could be considered in particular circumstances, yet are not widely recommended, or that have not been proven to provide significant benefits include systemic prophylaxis, antibiotic lock prophylaxis, systemic anticoagulation, and sutureless securement devices.

Peripherally inserted central catheters have been used for intermediate and long-term access in the acute care setting, and also for outpatient indications with low rates of associated BSI (70). In the ICU, they seem to have rates of infection comparable to nontunneled short-term central venous catheters, and for that reason their use should not be expected to result in decreased incidence of BSI (71–74).

Experience, education, and standardization seem to provide the best chance in terms of an institutional-wide decrease in rates of BSIs, and several reports of the creation of specialized "intravenous teams" responsible for the care of central catheters showed promising results. The Institute for Healthcare Improvement has condensed some of these measures into a central line (catheter) bundle, a core component of the 100,000 Lives Campaign, and the 5000,000 Lives campaign. It includes five key components (75):

1. Hand hygiene
2. Maximal barrier precautions
3. Chlorhexidine skin antisepsis
4. Optimal catheter site selection
5. Daily review of catheter necessity, with prompt removal

The implementation of this bundle has resulted in a very significant decrease in the rate of CLABSI in multiple institutions according to the Institute for Healthcare Improvement, and several peer-reviewed publications (76, 77).

Diagnosis

Systemic findings suggesting sepsis should raise the suspicion of CRBSI in any ICU patient with indwelling catheters; these include fever (which may be the only manifestation), hemodynamic instability, altered mental status, or new organ dysfunction. Local findings, or the presence of complications secondary to BSI like endocarditis, osteomyelitis, and metastatic infections are more specific but considerably less sensitive. Confirmation requires paired blood cultures following the criteria described above, with the exception of clinical sepsis in neonates and infants (15, 57).

Management

In the ICU, the management of CRBSI starts before the diagnosis has been confirmed, because decisions regarding the catheter (exchange, removal, or salvage) and antimicrobials should be made at the time of suspicion, particularly in patients with worsening clinical condition, where the catheter should be removed immediately, and antimicrobial therapy should be initiated. In more stable patients, both interventions still should be considered, including removal or catheter exchange over a guidewire and empirical antibiotics as the cultures are being processed.

Once a CRBSI has been confirmed, the clinical condition of the patient, the identified pathogen, and the type of catheter all have to be taken into account when deciding on therapeutic options. Catheter salvage may be attempted in uncomplicated CRBSI involving long-term catheters secondary to pathogens other than *S. aureus*, fungi, mycobacteria, *P. aeruginosa*, or other EDR Gram-negative bacilli. Systemic therapy with or without antimicrobial lock therapy can be used for the duration of the treatment, depending on the microorganism. Cultures 72 hrs after initiation of antibiotics should be negative in order to continue the attempt to salvage the catheter (58).

When *S. aureus* is identified, successful salvage is very unlikely and should only be attempted under extraordinary circumstances; treatment should be instituted for at least 14 days, and a high index of suspicion maintained for endocarditis and other complications. A transesophageal echocardiogram is indicated unless there is complete clinical and bacteriologic resolution within 72 hrs in a patient without risk factors for endocarditis other than the removed central catheter.

Antifungal therapy and catheter removal are needed for all cases of CRBSI due to *Candida* species. There has been very limited success in attempts to use antifungal lock therapy with amphotericin B or echinocandins for catheter salvage, and it is currently not recommended. The Infectious Diseases Society of America has published comprehensive evidence-based guidelines for the management of CRBSI, including the specific scenarios of hemodialysis patients, pediatric patients, short-term catheters, tunneled lines, and others (58).

Venous Thromboembolism

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are the two clinical manifestations of venous thromboembolism (VTE). Most thrombi are asymptomatic and confined to the deep veins in the calf, but when left untreated, 20% to 30% will extend to the thigh where they pose a 40% to 50% risk of embolization to the pulmonary circulation. VTE remains the most common preventable cause of hospital death associated with 50,000–100,000 deaths per year in the United States (78–82).

It is remarkable that a large number of fatal PEs and DVTs identified in postmortem examinations had not been suspected clinically. The ICU population is particularly susceptible; many of the patients already have thrombi before being transferred to the unit, with a prevalence on admission of 2% to 10%, and during the ICU stay, the incidence of new onset DVT is 9% to 40% (83).

Risk factors

VTE usually presents in the setting of one or more well-recognized risk factors within the context of Virchow's triad (i.e., stasis, endothelial injury, and hypercoagulable state) (84). For example, a population-based study in Worcester, MA, showed that the six most prevalent predictors of VTE were: immobility; recent or current hospitalization; recent surgery; malignancy; and recent infection (85). Other known factors include trauma, increasing age, pregnancy, contraceptives, obesity, respiratory failure, inflammatory bowel disease, nephrotic syndrome, central venous catheterization (including peripherally inserted central catheters), and inherited or acquired thrombophilia, among others (86).

The association of VTE with surgery has been long recognized, and risk stratification efforts have demonstrated an incidence of fatal PE without prophylaxis of 0.1% to 0.8% in elective general surgery, 2% to 3% after elective total hip replacement, and 4% to 7% after surgery for a fractured hip (87). In consequence, patients in surgical and trauma ICUs constitute a very high-risk population, and it is not surprising that VTE/PE rates are prominent in the morbidity and mortality figures of these units. On the other hand, bleeding risks are also increased due to surgery, trauma, thrombocytopenia, coagulopathy, and drugs, such as antiplatelet agents; and renal function is often abnormal, making the use of pharmacologic thromboprophylaxis challenging, and many times altogether unadvisable, even though the number of patients with true absolute contraindications is really small. Mechanical prophylaxis can be difficult as well, particularly in the setting of bilateral lower-extremity trauma, burns, or major leg surgery.

Prevention

Considering the mortality, morbidity, chronic sequelae, and resource utilization associated with VTE, our first approach must be prevention. Known risk profiles allow appropriate targeting of the population that would benefit the most, and we have accumulated solid evidence of improved outcomes associated with the use of pharmacologic and mechanical thromboprophylaxis in many different clinical settings. The ICU demands a formal and unique approach to thromboprophylaxis. On admission, all patients should be assessed for risk of VTE and risk of bleeding. Current guidelines from the American College of Chest Physicians recommended routine thromboprophylaxis, with low-molecular-weight heparin (LMWH) or low-dose unfractionated heparin for patients at moderate risk, with LMWH for patients at high risk, and with graduated compression stockings and/or intermittent pneumatic compression for those with significant risk of bleeding until it is safe to start LMWH (86). Optimization of the dosage of LMWH may require anti-Xa levels, particularly in patients with altered renal function, subcutaneous edema, or receiving pressors.

Compliance with thromboprophylaxis guidelines in critically ill patients has

been evaluated by a few utilization reviews and ranges from 50% to 80% of patients without absolute contraindications to receiving unfractionated heparin or LMWH. The physicians' willingness to prescribe anticoagulant prophylaxis is probably related to their assessment of risk of VTE, and risk of bleeding, but an institutional adoption of a formal thromboprophylaxis strategy has a clear effect in the number of patients who receive these medications. To be fair, it is important to point out that the scientific evidence about effectiveness and safety of pharmacologic thromboprophylaxis in surgical ICU patients has been largely extrapolated from the acute care setting. There are more data in the trauma literature because units caring for severely injured patients with high risk for VTE have adopted strict prophylaxis protocols that include the use of LMWH and have documented a low incidence of clinically significant bleeding events and positive impact on outcomes. The clinical use of LMWH and unfractionated heparin in medical-surgical ICUs is the subject of current randomized trials, and still further trial data are required to guide the optimal use of anticoagulant and mechanical prophylaxis in the critical care setting (88).

Diagnosis

VTE offers a true clinical challenge; significant clot burden may be silently present, signs and symptoms when present are often nonspecific, and in some unfortunate cases, the first evidence of this condition might be a sudden and irreversible hemodynamic collapse. It is, thus, very important to maintain a high index of suspicion, and to keep in mind the risk profile of our patients.

DVT presents with swelling, pain, and discoloration in the involved extremity. Physical examination may reveal warmth, a palpable cord, superficial venous dilation, and unilateral edema. These findings have traditionally required confirmation with contrast venography (gold standard); more recently, magnetic resonance venography has been found to be equally accurate. Currently, however, duplex ultrasonography is the modality of choice, given its combination of sensitivity, specificity, and safety. Other less sensitive and specific diagnostic modalities include impedance plethysmography and fibrinogen I-125 scanning (89).

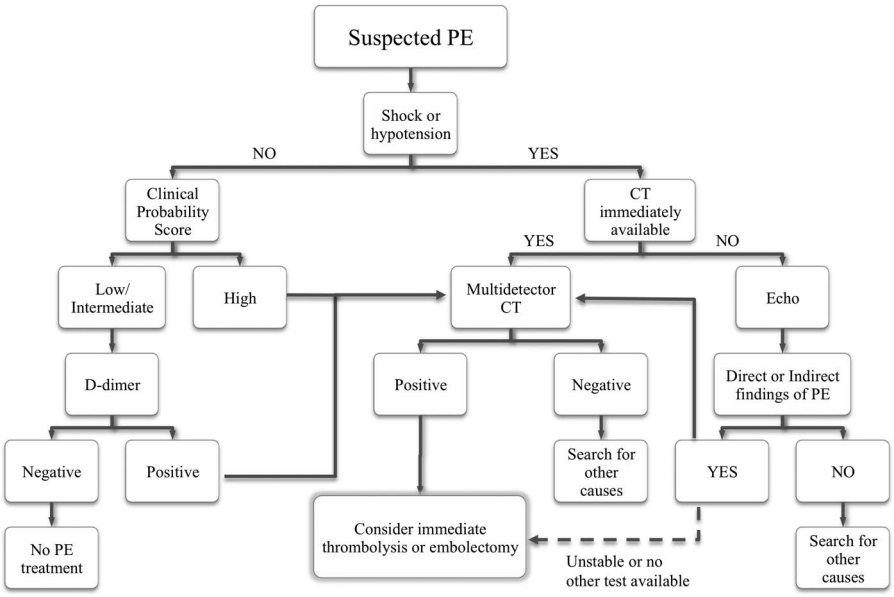

Figure 5. Diagnostic and therapeutic algorithm for the management of the patient with suspected pulmonary embolism (*PE*), recommended by the European Society of Cardiology guidelines (2008). *CT*, computed tomography. Adapted with permission from Torbicki et al (93).

Classically, patients with PE complain of dyspnea, pleuritic chest pain, cough, hemoptysis, and on phyisical examination are found to be tachypneic, tachycardic, with rales, gallop, accentuated pulmonic component of S2, and sometimes circulatory collapse. Electrocardiography findings (S1Q3T3 pattern, right ventricular strain, right bundle branch block) might suggest PE but are common in patients with other reasons for chest pain or dyspnea. Chest radiography is frequently abnormal, but very unspecific, and this is also true for arterial blood gases, troponin, and brain natriuretic peptide. Confirmation requires pulmonary angiography, and in some centers with good experience, spiral computed tomography pulmonary angiography is widely used, reaching comparable sensitivity and specificity. When contrast angiography is not available or contraindicated, therapeutic decisions could be made based on echocardiography, V/Q scan, D-dimer, lower-extremity ultrasound, all with the help of clinical criteria like the Wells Clinical Probability Score, or the revised Geneva Score (90–92).

Treatment

The objectives of treatment in patients with DVT are prevention of PE, clot extension, recurrence of thrombosis, and the development of late complications. Anticoagulation therapy initially with unfractionated heparin or LMWH, then followed with warfarin for 3 to 6 months, is usually recommended. For severe cases, like phlegmasia cerulea dolens, thrombolytic therapy and/or thrombectomy should be considered.

In a patient with suspected PE, the initial focus is stabilization, including respiratory and hemodynamic support. If the index of suspicion is high, empirical anticoagulation should be started during the resuscitation. Diagnostic evaluation must be completed as soon as possible. Once a PE has been confirmed, thrombolytic therapy should be considered in patients with hemodynamic instability; if there is no improvement or thrombolysis is contraindicated, then surgical or catheter embolectomy may be attempted. Figure 5 is an example of the proposed diagnostic and management algorithm, in an institution with multidetector computed tomography scanner, as recommended by the European Society of Cardiology in the 2008 guidelines on PE (93).

In the ICU, inferior vena cava filters are only indicated in patients who cannot receive anticoagulants and have a confirmed proximal DVT, to prevent the occurrence or recurrence of PE. Inferior vena cava filters have been used prophylactically in very high-risk patients, like multisystem trauma with pelvic or long-bone fractures, but the ACCP guidelines do not support this indication, due to lack of solid evidence demonstrating de-

creased prevalence of PE, survival benefit, or cost-effectiveness (86).

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