Preventing Catheter-Related Bloodstream Infections outside the Intensive Care Unit: Expanding Prevention to New Settings

Alexander J. Kallen, Priti R. Patel, and Naomi P. O’Grady

Bloodstream infections (BSIs) are a potentially life-threatening health care–associated infection (HAI). Although the true incidence of BSIs is not known, an estimated 250,000 health care–onset BSIs occurred in the United States in 2002, resulting in >30,000 deaths [1]. Most of these health care–onset BSIs are associated with the presence of a central venous catheter (CVC) [2–4]. Although the attributable mortality due to catheter-related BSIs (CRBSIs) is not clear, these infections have been associated with higher costs, crude mortality rates, and number of hospital-days [5, 6].

CRBSIs continue to be associated with considerable morbidity and mortality; however, results from several collaboratives have demonstrated the preventability of these infections in intensive care units (ICUs) [7, 8]. To date, prevention efforts have focused on ICUs for several reasons, including the presence of a well-delineated patient population and staff, the high prevalence of CVC use in these settings, and the profound effect of HAIs among this patient group [9]. The success of these efforts has raised interest in expanded CRBSI prevention efforts. The US Department of Health and Human Services HAI Plan includes as one of its 5-year targets a 50% decrease in the rate of BSIs among patients with central lines, including in non-ICU settings [10]. In this review, we will describe what is known about the epidemiology of CRBSIs outside the ICU and discuss recommended measures for preventing these infections.

EPIDEMIOLOGY

Acute care. Although much of our understanding of CVC use in acute care settings comes from studies conducted in the ICU, recent data have begun to better define the use of CVCs in other parts of the hospital. The proportion of patients with CVCs has generally been lower in non-ICU settings than in ICUs; however, the total burden of CVC use might be greater outside the ICU. In the National Healthcare Safety Network (NHSN) report for 2009, the proportion of patient-days classified as central line–days (ie, patient has 1 or more CVCs on that day) for medical-surgical ICUs was between 39% and 59%, compared with 16% for medical-surgical wards [11]. In a survey among hospitals that are part of the Centers for Disease Control and Prevention’s Epicenter Program, the proportion of patients...
in the ICU with a CVC was 55%, compared with 24% of patients in wards [12]. However, because more total patients were outside the ICU than in the ICU, the majority of patients with CVCs were outside the ICU (70%). In addition, catheters may be in place longer in patients outside the ICU. In one study, dwell times were longer in medicine wards (median, 6 days) and surgical wards (median, 8 days) than in ICUs (median, 5 days) [13].

CVC types and the site of insertion appear to vary between ICUs and wards [12]. In a survey of 6 academic tertiary-care medical centers, jugular and femoral catheters were more commonly used in the ICU, whereas peripherally inserted central catheters and subclavian catheters were more common outside the ICU [12]. In the ICU, 74% of CVCs were nontunneled, compared with ~33% outside the ICU. Unnecessary use of CVCs also might be more common outside the ICU. In a cross-sectional evaluation at one large public hospital, unjustified CVC-days were more common outside the ICU (9% vs 2%) [14].

CVC care also might vary between ICUs and non-ICUs [14, 15]. In a prospective audit at one facility, breaches in care were more likely to occur in non-ICU settings than in the ICU [15]. In another evaluation, more lapses in CVC care, demonstrated by the presence of a nonintact dressing, were identified among non-ICU patients than among ICU patients [14].

A number of issues complicate comparisons of device utilization and BSI rates between wards and ICUs. First, patients often spend time in >1 hospital unit during their admission, and these patients could have their CVCs placed outside the unit in which they are admitted when surveillance is done, thereby complicating the attribution of infections [9, 13]. In one study, 71% of CVCs in ICU patients were placed in the ICU, but only 14% of CVCs in medical ward patients were placed there [13]. Second, the types of CVCs used vary between studies and settings, and the rates of BSIs associated with different CVCs appear to differ, with lower rates generally found for tunneled catheters than for nontunneled catheters [16]. Third, BSI definitions also vary between studies, making rate comparisons more difficult. Rates identified using surveillance definitions, such as the definition of central line–associated BSI (CLABSI) used in the NHSN [17], are often simpler to use but might overestimate the true rate of BSIs due to CVCs. Clinical definitions, such as that used for CRBSI, have criteria designed to more strongly implicate the CVC as the cause of the BSI but rely on measures that are more difficult to obtain, such as time to culture positivity, quantitative blood cultures, or semiquantitative catheter tip cultures [18]. In this review, when describing BSI rates we have used the term CRBSI for studies that used clinical definitions or when referring specifically to infections that are due to the catheter and the term catheter-associated BSI (CABSI) when surveillance definitions were used or when referring to infections that occur in patients with catheters when the catheter has not been clearly shown to be the ultimate source of the infection.

Several studies have evaluated the rates of BSIs among inpatients with CVCs [11, 19, 20]. In a prospective review at one teaching hospital, the CABSI rate in the medical wards (5.7 cases per 1000 catheter-days) was similar to the rate in the medical ICU during the same period (5.2 cases per 1000 catheter-days) [19]. Another study from the German Nosocomial Infection Surveillance System found that the CABSI rate in non-ICU settings (4.3 cases per 1000 catheter-days) was actually higher than that reported to the surveillance system from ICUs (1.8 cases per 1000 catheter-days) [20]. CABSI rates in that study were similar between internal medicine wards (4.4 cases per 1000 catheter-days) and surgical wards (4.7 cases per 1000 catheter-days). In the NHSN, differences in CABSI rates between wards and ICUs vary depending on the types of units and the teaching status of the facility [11]. However, in the 2009 report the pooled mean CABSI rate for the 617 reporting medical-surgical wards was 1.2 cases per 1000 catheter-days, which was slightly lower than the rate seen for medical-surgical ICUs (1.5 to 2.1 cases per 1000 catheter-days).

A summary of differences in rates of CABSIs between ICU and non-ICU settings is shown in Table 1.

Ambulatory care. In addition to their important role in acute care, chronic CVCs are also commonly used in patients who receive their medical treatment primarily as outpatients, such as those receiving hemodialysis, oncology treatment, or parenteral nutrition. Approximately 25% to 30% of all hemodialysis patients nationally use a CVC for dialysis, and ~80% of patients initiate hemodialysis with a CVC [21–23]. Furthermore, an estimated two-thirds of cancer patients use a long-term tunneled CVC [24].

As in acute care facilities, CRBSIs can also complicate use of CVCs in outpatient settings. In one study of patients with BSIs at 1 of 3 hospitals in North Carolina, 37% of BSIs were attributed to outpatient exposures to health care [25]. Intra-vascular devices were the most common source of these infections. Among all hemodialysis patients in the US End Stage Renal Disease Program, rates of hospitalization for infections increased 34% from 1993 to 2006, a time when rates of hospitalization for other common diagnoses decreased [21]. BSI hospitalizations remain among the greatest contributors to infectious hospitalizations for hemodialysis patients (103 admissions per 1000 patient-years in 2006). In addition, rates of hospitalization for vascular access infections increased >100% during the same period.

CABSI rates among outpatients are difficult to generalize, because reported rates vary. Rates are influenced by a number of factors, including patient comorbidities, catheter type, and CVC indication. In a study of >50,000 home health patients...
Table 1. Summary of Reported Epidemiology of Central Line Use and Rates of Catheter-Associated Bloodstream Infections Inside and Outside Intensive Care Units (ICUs)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Wards</th>
<th>ICUs</th>
</tr>
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<tbody>
<tr>
<td>Patients with CVCs, a %</td>
<td></td>
<td></td>
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<tr>
<td>Estimate 1 [12]</td>
<td>24</td>
<td>55</td>
</tr>
<tr>
<td>Estimate 2 [20]</td>
<td>5</td>
<td>69</td>
</tr>
<tr>
<td>CVC insertion site, % [12]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Femoral</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Internal jugular</td>
<td>17</td>
<td>33</td>
</tr>
<tr>
<td>Subclavian</td>
<td>61</td>
<td>47</td>
</tr>
<tr>
<td>Peripherally inserted</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>CVC types, % [12]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nontunneled</td>
<td>33</td>
<td>74</td>
</tr>
<tr>
<td>Peripherally inserted, tunneled, or totally implanted</td>
<td>67</td>
<td>26</td>
</tr>
<tr>
<td>Duration of CVC use, median days (IQR) [13]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical-surgical units</td>
<td>6 (3–15)b</td>
<td>3 (2–6)</td>
</tr>
<tr>
<td>Medical units</td>
<td>8 (4–14)c</td>
<td></td>
</tr>
<tr>
<td>Surgical units</td>
<td>0.16</td>
<td>0.39–0.59</td>
</tr>
<tr>
<td>Pooled mean CVC utilization ratio d [11]</td>
<td>0.20</td>
<td>0.45–0.61</td>
</tr>
<tr>
<td>Pooled mean CLABSI rate, cases per 1000 CLDs e [11]</td>
<td>1.2</td>
<td>1.5–2.1</td>
</tr>
<tr>
<td>Medical-surgical units</td>
<td>1.5</td>
<td>1.9–2.6</td>
</tr>
<tr>
<td>Medical units</td>
<td>1.4</td>
<td>2.3</td>
</tr>
<tr>
<td>Surgical units</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** CLABSI, central line–associated bloodstream infection; CLDs, central line–days; CVCs, central venous catheters; IQR, interquartile range.

- a The first estimate is from a 1-day multicenter point-prevalence survey in the United States, and the second estimate is from a multicenter surveillance system in Germany and reflects the percentage of patient-days with a CVC.
- b, c Medical wards.
- d Defined as the no. of CLDs per the no. of patient-days. Ranges are used because data for those units are stratified by facility teaching status and/or bed size.
- e Ranges are used because data for some units are stratified by facility teaching status or facility teaching status and bed size.

with a wide variety of diagnoses and several different catheter types, the rate of BSIs was 0.19 cases per 1000 catheter-days [26]. In another multisite study of patients receiving home infusion therapy for diverse indications, the BSI rate was 0.99 cases per 1000 catheter-days [27]. Among outpatient hemodialysis facilities reporting to the NHSN, the pooled mean rate of BSI among patients with permanent CVCs was 4.2 cases per 100 patient-months (roughly 1.4 cases per 1000 catheter-days) [23]. Higher BSI rates among hemodialysis patients with CVCs have been reported in trials of antimicrobial locks (3–4 cases per 1000 catheter-days) [28]. Because patients with malignancies often have a variety of CVC types and could frequently transition between the inpatient and the outpatient setting, determining absolute rates of CABSIs is difficult. In one review of infectious complications in cancer patients with long-term CVCs, CRBSI rates were 2.14 cases per 1000 catheter-days for catheters and 0.09 cases per 1000 catheter-days for implanted ports [29].

**PREVENTION**

Preventing CRBSIs outside the ICU requires an understanding of the mechanisms by which catheters become infected as well as knowledge of currently recommended infection prevention interventions. The recommendations for many interventions are based on studies conducted in ICUs, and the generalizability of these results outside of ICUs and for longer-term CVC use is not well known. A complete description of prevention practices is beyond the scope of this review; however, several different practice recommendations are available, including the Centers for Disease Control and Prevention/Healthcare Infection Control Practices Advisory Committee’s Guidelines for the Prevention of Intravascular Catheter-Related Infections, which are scheduled for an update in 2010, and the Society for Healthcare Epidemiology of America/Infectious Disease Society of America’s Strategies to Prevent CABSIs in Acute Care Hospitals [30, 31].
**Pathogenesis.** There are 4 main routes by which CVCs become colonized: from bacteria contaminating the outside of the catheter either at the time of insertion or after insertion (extraluminal); by contamination of the hub, catheter, or other administration device (intraluminal); or, less commonly, via infusion of contaminated solutions or hematogenous seeding from bacteremia from another source [32]. After colonization of the catheter, bacteria can adhere and form biofilm and subsequently disperse into the bloodstream, leading to CRBSI [33].

Evidence suggests that the extraluminal pathway predominates in the first week after CVC placement, whereas the intraluminal mechanism is the more common pathway for CVCs that are ≥1 week old [32, 34]. In a study that examined catheters for biofilm, the presence of biofilm was greater on the external surface of the catheter for those in place <10 days, and biofilm on the luminal surface surpassed that on the external surface for catheters in place >30 days [34]. In one study of short-term catheters, a CRBSI was considered to be extraluminally acquired if there was concordance between isolates cultured from the catheter tip, skin segment, and blood and was considered to be intraluminally acquired if there was discordance between cultures for the hub or infusate and the blood. Using this criteria, it was determined that 60% of CRBSIs were extraluminally acquired, 12% were intraluminally acquired, and 28% were indeterminate [32]. These findings suggest that interventions focused around CVC insertion, which primarily target the extraluminal route of infection, might be expected to have a large effect on CRBSIs in the ICU, where catheter dwell time might be shorter. Although optimizing catheter insertion practices remains important outside the ICU, additional attention to catheter maintenance to prevent infections that develop via the intraluminal route might be required.

**Interventions.** Facilities providing care to patients with CVCs should first ensure that staff members responsible for the insertion and maintenance of CVCs have received appropriate training and that they have demonstrated competence to perform these functions. Educational interventions designed to improve knowledge about recommended procedures have been shown to decrease rates of CABSIs [35]. Periodically measuring adherence to CVC insertion and maintenance practices and providing these results back to the staff might help promote adherence to recommended procedures. In addition, CABSIs surveillance is important. Collecting infection rates with feedback of this information to staff has been shown to decrease BSI rates in a study of dialysis patients [36]. Understanding facility CVC use and CABSIs rates also might help guide intervention efforts. Currently, the NHSN offers modules to conduct CABSIs surveillance in ICUs, inpatient wards, and outpatient hemodialysis centers as well as a module to collect information on central line insertion practices.

In addition to training, education, and surveillance, important prevention practices include the use of chlorhexidine skin antiseptics and maximal sterile barrier precautions (including gown, sterile gloves, cap, mask, and a full-body drape) at catheter insertion [37, 38]. Ensuring that all necessary supplies are readily available (eg, in one cart or kit) may be one way to improve adherence to this recommendation [39]. When considering insertion practices, particularly for patients outside the ICU, addressing adherence is necessary in all areas of the hospital in which catheters are placed (eg, emergency department, operating room, and interventional radiology) and not just on the wards in which surveillance is being conducted.

In general, the femoral site should be avoided for nontunneled CVCs to prevent infection [40]. However, subclavian vein catheterization should particularly be avoided in patients with renal failure, because of the risk of subclavian vein stenosis [41]. In addition, to preserve future vascular access options it has also been suggested that upper-extremity peripherally inserted central catheters and nondialysis subclavian CVCs be avoided not only for those with end-stage renal disease but also for patients with chronic kidney disease who might require dialysis.

Ensuring the use of appropriate CVC maintenance practices is also an important part of preventing CRBSI. Maintenance practices might be particularly important outside the ICU, where CVCs could be used for longer periods [13]. Interventions designed to facilitate the removal of unnecessary catheters are fundamental to decreasing these infections and has been an important part of collaboratives to reduce CABSIs in the ICU [8]. For individual patients, regularly evaluating the need for CVCs, including when moving out of the ICU, might be one way to ensure that unnecessary catheters are promptly removed [39].

Other important maintenance practices recommended in current guidelines include use of hand hygiene before handling catheters or catheter sites, use of chlorhexidine for skin antisepsis with dressing changes, and disinfecting catheter hubs or injection ports with an appropriate agent before accessing the catheter [30, 31]. Use of certain types of mechanical valve needleless connectors has been associated with higher rates of BSI in some observational studies [42, 43]. As more work is done to understand these associations, facilities using implicated needleless connectors should do so with strict adherence to the manufacturers’ recommendations when caring for and maintaining these devices and should closely monitor BSI rates. Among patients undergoing hemodialysis, application of a topical antimicrobial ointment (povidone iodine or bacitracin, gramicidin, and polymyxin B) to the exit site during dressing changes is also recommended to decrease rates of CLABSI [44, 45]. Ointments are not recommended for nonhemodialysis patients because of concerns about promoting fungal infections and antimicrobial resistance [46, 47].
In addition to the practices to prevent CABSIs described above, several additional interventions might play a role in facilities where adherence to core interventions has not resulted in decreases in CABSIs rates to facility goals. Antimicrobial-impregnated catheters, including those coated with antiseptics, have been evaluated in a number of trials and meta-analyses and have been shown to reduce the risk of CVC colonization and/or CRBSI versus noncoated catheters [48–50]. They can be considered as a supplemental intervention in patients with catheters that are expected to remain in place for >5 days. Chlorhexidine bathing in the ICU has been shown to decrease CABSIs rates and might be considered for use outside the ICU [51]. A chlorhexidine-impregnated sponge dressing has demonstrated efficacy in preventing CRBSIs, including in a recent large randomized trial in ICUs [52], and can also be used as a supplemental intervention. The use of antimicrobial catheter locks, including the use of nonantibiotic antiseptic locks (such as alcohol or trisodium citrate), have also demonstrated some success in reducing CRBSIs and have the potential to minimize the intraluminal route of catheter colonization [28, 53]; however, catheter locks require more evaluation before they can be recommended for widespread use.

SUMMARY AND FUTURE DIRECTIONS

As successes are being realized in preventing CABSIs in ICUs, it is now recognized that a substantial number of these infections occur outside the ICU. This is true not only in hospital wards, where CABSIs rates appear to be similar to those found in ICUs, but also among subgroups of outpatients who require long-term CVCs as part of their care. To better understand CABSIs, systematic surveillance for these infections should include non-ICU acute care and outpatient settings. Further investigation and development of surveillance methodologies will be needed to more clearly establish the best ways to collect and interpret BSI rates outside of ICUs. More work is also needed to better define the burden and epidemiology of CRBSIs in non-ICU settings, particularly among outpatients. In an era of tightening budgets, this will be challenging but important work. These efforts may also require new partnerships between infection prevention and other groups, such as nephrologists, oncologists, or nursing staff from hospital wards.

Finally, a better understanding of the relative effectiveness and generalizability of CRBSI prevention interventions is required. Identifying the contribution of individual interventions is important in determining whether each component is cost-effective and clinically meaningful. For example, if chlorhexidine is used as a skin antiseptic, how does the addition of a chlorhexidine-impregnated sponge dressing contribute to the reduction in infection rates? In addition, it will be necessary to delineate effective CVC maintenance “bundles,” which may be particularly important for patients with long-term CVCs, as well as develop and test new intervention technologies. However, as rates of CABSIs have decreased over the past decade, studying novel interventions to reduce these infections has become more challenging. Given the low infection rates that have been achieved in ICUs when recommended prevention methods have been instituted, substantial effort now needs to be focused not only on evaluating these interventions further but on expanding strategies to promote adherence to proven interventions, particularly in non-ICU settings.

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