OBSERVATIONAL STUDY

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Evaluating the Adequacy of Central Line-Associated Bloodstream Infection As a Quality Measure: A Cross-Sectional Analysis at a Single Tertiary Care Center

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IMPORTANCE: The current definition of central line-associated bloodstream infection (CLABSI) may overestimate the true incidence of CLABSI as it is often unclear whether the bloodstream infection (BSI) is secondary to the central line or due to another infectious source.

OBJECTIVES: We aimed to assess the prevalence and outcomes of central CLABSI at our institution, to identify opportunities for improvement, appropriately direct efforts for infection reduction, and identify gaps in the CLABSI definition and its application as a quality measure.

DESIGN, SETTING, AND PARTICIPANTS: Retrospective cross-sectional study of patients identified to have a CLABSI in the period 2018–2022 cared for at the value-based purchasing (VBP) units of a 1200-bed tertiary care hospital located in Cleveland, OH. Each CLABSI episode was assessed for relationship with central venous catheter (CVC), suspected secondary source of BSI, mortality associated with the CLABSI hospital encounter, and availability of infectious disease physician or primary physician documentation of infectious source.

MAIN OUTCOMES AND MEASURES: CLABSI episodes were classified as CVC related, CVC unrelated, and CVC relationship unclear. Mortality during the same encounter as the CLABSI event was assessed as an outcome measure. Descriptive statistics were performed.

RESULTS: A total of 340 CLABSI episodes occurred in adult patients in VBP units. Majority of the CLABSI, 77.5% (266), occurred in the ICU. Of the CLABSI analyzed, 31.5% (107) were classified as unrelated to the CVC; 25.0% (85) had an unclear source; 43% (148) were classified as CVC related. For CVC-related cases, *Staphylococcus* and *Candida* were the predominant organisms. For the CVC unrelated and unclear groups *Enterococcus* was most prevalent. The mortality rate was lowest among patients classified with a CVC-related BSI. The positive predictive value (PPV) of the Centers for Disease Control and Prevention CLABSI definition to predict a true CVC-related infection was found to be 58.0%.

CONCLUSIONS AND RELEVANCE: The definition of CLABSI as a surrogate for catheter-related BSI is inadequate, with a PPV of 58.0% (43.1–67.6%). Efforts should be redirected toward revising the CLABSI definition and possibly reevaluating its criteria. Resources should be assigned to further investigate and systematically prevent BSIs from secondary sources while adhering to existing CLABSI prevention bundles.

KEYWORDS: central venous catheterization; critical care; healthcare quality; healthcare-associated infection; nosocomial infection

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KEY POINTS

Question: We hypothesized that not all central line-associated bloodstream infection (CLABSI) cases are solely attributable to central venous catheter (CVC), and there is a gap in the predictive value of the surveillance definition of CLABSI and the clinical impression of the sources of CLABSI.

Findings: Out of the 340 CLABSI episodes, 31.5% (*n* = 107) were classified as unrelated to the CVC, 25.0% (*n* = 85) of CLABSI episodes had an unclear source, and 43% (*n* = 148) of the CLABSI episodes were classified as CVC related. The positive predictive value (PPV) of the National Healthcare Safety Network/Centers for Disease Control and Prevention CLABSI definition (148/255) to predict a true CVC catheter-related infection, based on clinical reviews, is 58.0% (43.1–67.6%).

Meaning: The PPV of CLABSI for clinical purposes and as a quality metric is low, thus efforts should be redirected towards using CLABSI as a surveillance definition only and possibly reevaluating its inclusion and exclusion criteria.

Central venous catheter (CVC) or central line-associated bloodstream infection (CLABSI) is a rare, but devastating event for hospitalized patients, especially in the ICU. The adverse outcomes related to CLABSI include increased mortality rates, prolonged duration of hospitalization, and reduced reimbursement from Medicare (1). The National Healthcare Safety Network (NHSN) defines CLABSI as a primary bloodstream infection (BSI) that develops in a patient with a central line in place within the 48-hour period before onset of the BSI that is not related to infection at another site (2, 3).

The validity of a definition developed originally for surveillance but now known mainly as a quality metric and to drive clinical practice changes is questionable (4–6). The use of this definition may overestimate the true incidence of CLABSI as it is often unclear whether the BSI is secondary to the central line or due to another infectious source such as pneumonia, urinary tract infection, or abdominal abscess, despite many exclusion criteria (6–8). Catheter-related BSI (CRBSI) is a more rigorous diagnostic definition and requires specific laboratory testing to identify the catheter as the source of the BSI, such as culturing the catheter tip or a more elaborate method such as differential time-to-positivity of blood cultures (3, 6). But these methods to associate the infection with the catheter as the source are not routinely performed for this differentiation in clinical practice. Additionally, the CRBSI does not eliminate the possibility of secondary sources of infection seeding these catheters.

Substantial patient safety and quality improvement initiatives and spending efforts are directed at lowering CLABSI rates given the adverse outcomes associated with it, as well as the growing evidence that demonstrates that CLABSI infections are preventable (9). Furthermore, the Centers for Medicare and Medicaid Services assign financial penalties when CLABSI occurs by denying reimbursements for hospitals with high infection rates (10).

Decreasing CLABSI rates is one of the prioritized quality and safety objectives at our institution. Our institution has implemented several strategies to reduce CLABSI in compliance with the best practices related to the central-line bundle of insertion, maintenance, and removal. We hypothesize that the surveillance criteria used to identify CLABSI overestimate the true prevalence of CVC-related BSIs and that a considerable number of CLABSI cases are misidentified BSIs from other sources. We thus hypothesize that not all CLABSI cases are solely attributable to CVC, and there is a gap in the predictive value of the "surveillance" definition of CLABSI and the "clinical impression" of the sources of CLABSI. This is important as most of the efforts on eliminating CLABSI are focused on prevention of CVC as the source of infection. Focus on the CVC alone may reduce the opportunity to design interventions to address preventable CLABSIs originating from secondary BSIs.

We aimed to assess the prevalence and outcomes of CLABSI at our institution and to determine CLABSI cases that were falsely identified as BSI from CVC and estimate the positive predictive value (PPV) of the "surveillance" definition of CLABSI against the "clinical impression." We also postulated that the CVC-related CLABSIs should be easier to treat with removal of the catheter and administration of antibiotics relative to other complex infections. Our intended goals were to identify opportunities for improvement,

appropriately direct efforts for infection reduction, and identify gaps in the CLABSI definition and its application as a quality measure.

MATERIALS AND METHODS

Study Design, Setting, and Participants

This study is a single center, retrospective cross-sectional analysis. The patient population included adult patients (> 18 yr), hospitalized at the main campus of the Cleveland Clinic, a 1200-bed tertiary care center located in Cleveland, OH, between January 1, 2018, and December 31, 2022. The study population was identified using the institutional CLABSI database for quality improvement, and further analysis was performed using data from Epic, our institution's electronic medical record system. No Institutional Review Board (IRB) review was necessary because this study was not considered human subjects research by IRB guidelines.

Routine hospital-acquired bloodstream surveillance at Cleveland Clinic is performed prospectively and includes determination of CLABSI events as per NHSN definitions. Central line days and patient days are obtained from an electronic database and counted as per NHSN convention. The cohort consisted of consecutive patients identified as having a CLABSI event.

We examined the CLABSI episodes that occurred in the value-based purchasing (VBP) units of the hospital. The VBP program links Medicare payments and penalties to healthcare quality for areas that provide inpatient acute care services. The performance measures component of VBP includes specific areas of clinical care, person and community engagement, safety, efficiency, and cost reduction (1, 11).

Definitions and Interventions

After identification of the CLABSI events for review, we used a template to annotate the CLABSI episodes for the following: relationship with CVC, suspected secondary source of BSI, mortality associated with the CLABSI hospital encounter, and availability of infectious disease (ID) physician or primary physician documentation of infectious source. Information related to the organism causing the BSI was available in the CLABSI database.

First, we classified the CLABSI episodes into the following three classes: CVC related, CVC unrelated, and CVC relationship unclear. This was based on the reviews performed of the ID physician's clinical notes. CVC-related CLABSI events were those where the ID physician's clinical note inferred significant evidence of association of the BSI being directly related to CVC infection. CVC-unrelated CLABSI events were those where the ID physician's clinical note inferred significant evidence of association of the BSI being directly related to a non-CVC secondary source of infection, such as intra-abdominal or pulmonary.

Suspected secondary sources were then further classified based on the theorized origin as documented in the clinical note. For those events where the reviewers could not determine the suggested source of BSI based on their review of the ID physician's clinical note, the events were classified as CVC unclear. If there was no ID consultation documented, then we based our reviews on the primary physician's clinical note and impression. The majority of the CLABSIs did have an ID physician consultation and documentation.

Last, we noted if the patient had died during the same encounter as the CLABSI event to assess its impact on outcomes. Descriptive statistics were performed to analyze the available data. Python 3.9 was used as the programming language within Jupyter Notebook, Anaconda 4 (Anaconda, Austin, TX) to perform the analysis.

RESULTS

In our initial review, we evaluated 671 CLABSI episodes for our analysis. These occurred among 645 patients and in 58 different units (ICUs and non-ICUs) across Cleveland Clinic's main campus hospital. For our detailed analysis, we then selected the CLABSI episodes that had occurred in the VBP units only. The total number of CLABSI episodes in the VBP units was 343 in the same period, across 28 different units (ICUs and non-ICUs) across the main campus of the Cleveland Clinic (**Fig. 1**). The total central line-days were 352,583 over the study period.

The majority of the CLABSI events, 77.5% (266), occurred in the ICUs. We excluded three cases as they occurred in pediatric patients housed in these units, so the final analysis included a review of 340 CLABSI events. Some adult patients were in the PICU and floor during the CLABSI event and were included in the analysis.

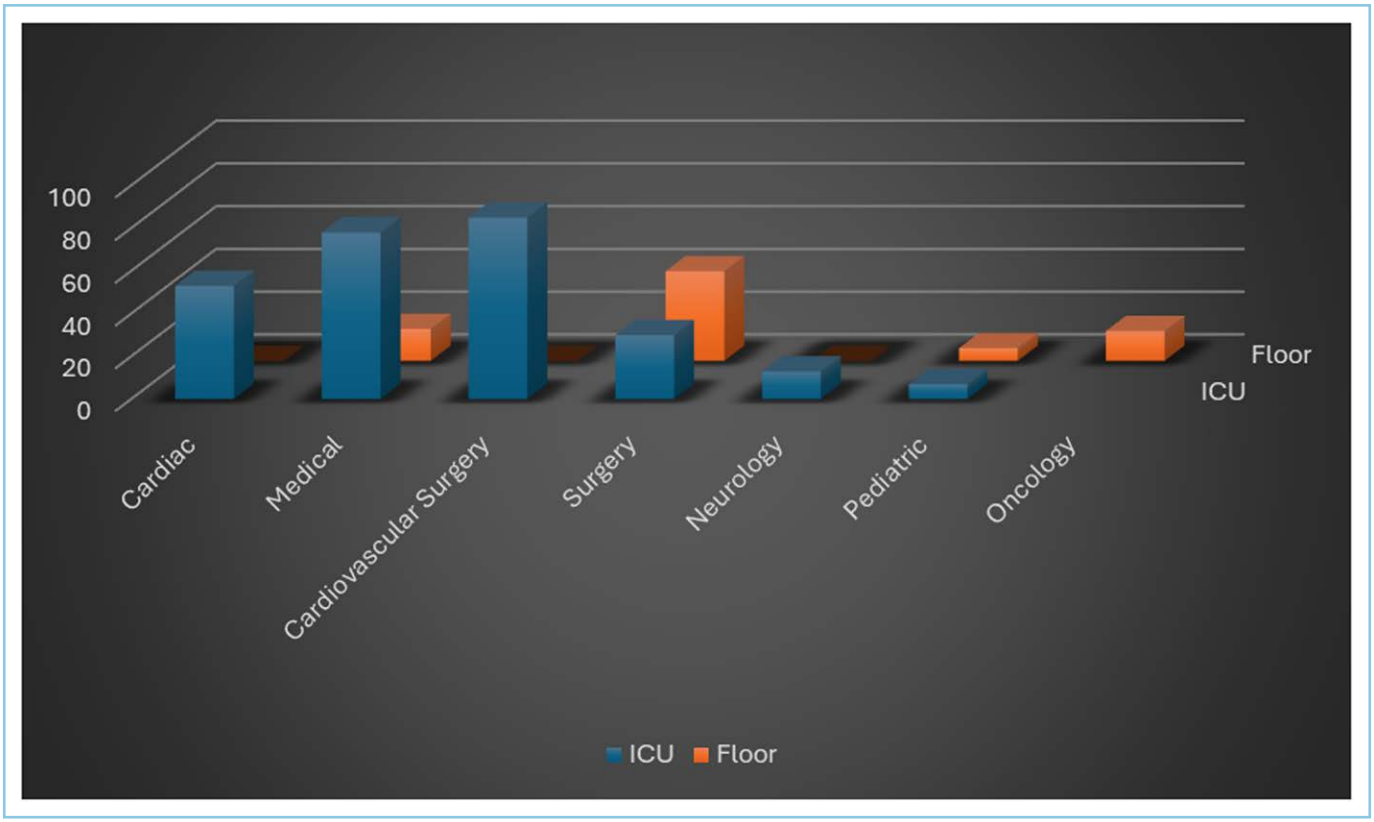

Figure 1. Distribution of central line-associated bloodstream infection events based on patient location.

CLABSI Association With CVC

Out of the 340 CLABSI episodes in VBP units, 31.5% (n = 107) were classified as unrelated to the CVC. To the clinicians reviewing based on the supportive documentation from the ID physicians taking care of the patients, 25.0% (n = 85) of CLABSI episodes had an unclear source. Forty-three percent (n = 148) of the CLABSI episodes were classified as CVC related, emphasizing the need to continue with the best practices related to CLABSI prevention (**Fig. 2**).

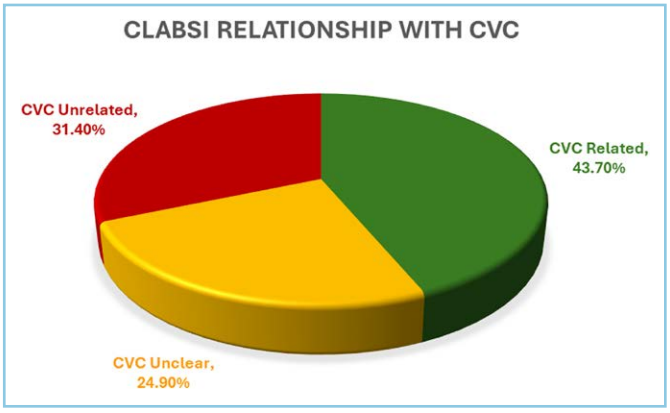

Figure 2. The distribution of central line-associated bloodstream infection (CLABSI) counts based on assessment of the relationship to a central venous catheter (CVC) as the infectious source.

Predictive Value of CLABSI Definition Based on Clinical Reviews

True positive CLABSI (CVC related) = 148

False positive CLABSI (CVC unrelated) = 107

Positive Predictive Value (PPV) = TP/TP + FP

where TP is true positive and FP is false positive.

The PPV of the NHSN/Centers for Disease Control and Prevention (CDC) CLABSI definition (148/255) to predict a true CVC-related infection, based on clinical reviews, is 58.0%. If all the CVC unclear CLABSI events were found to be CVC related, then the PPV would increase to 67.6% (148 + 85/340). Whereas, if all the CVC unclear CLABSI events were found to be CVC unrelated then the PPV would decrease to 43.1%. Thus, based on our analysis, the PPV of NHSN-CDC definition of CLABSI could range between 43.1% and 67.6%. This is not different from some of the earlier reported studies where CLABSI were compared with CRBSI (12).

Organisms Associated With CLABSI

Excluding culture results showing mixed flora, *Enterococcus*, *Staphylococcus*, and *Candida* were the predominant organisms found among all the CLABSI events. For CVC-related cases, *Staphylococcus* and *Candida* were the predominant organisms. For the CVC unrelated and unclear groups *Enterococcus* was most prevalent (**Fig. 3**).

Secondary Sources of CVC-Unrelated CLABSIs

Gastrointestinal and pulmonary were the key alternative sources of CLABSI episodes based on the reviews of ID physician clinical notes (**Fig. 4**). Of the 107 CL-unrelated BSI cases, 40 CLABSI events (37%) were found to be of gastrointestinal origin, 28 (26.1%) of pulmonary in origin, and 13 of genitourinary origin (12.1%).

Association of CLABSI With Mortality

The mortality rate among the patients with CLABSI was lowest among patients classified with a CVC-related BSI and highest in patients in whom the source of BSI was unclear, 44 (39%) vs. 38 (67%), respectively (**Fig. 5**). The CVC-unrelated group, with 57 patients, had a mortality rate of 53%.

DISCUSSION

Based on our analysis, 31.5% of events initially classified as CLABSI were clearly caused by another infectious source, suggesting that the current CLABSI definition may no longer remain accurate. Another 24.9% of the CLABSIs had a lack of a clear source based on the ID physicians' review and documentation. Previous CLABSI prevention efforts have focused on CVC insertion and care bundles (13–15). CVC insertion and care bundles need to be adhered to, as even at our institution despite strict adherence to these bundles, there are CLABSI events which are clearly CVC related (43%) (16). However, focusing solely on CVC insertion and care bundles may not further reduce CLABSI rates as there were 31.5% of CLABSI cases at our institution that were found to be unrelated to a CVC.

The definition of CLABSI is especially important to help identify this serious condition and implement effective

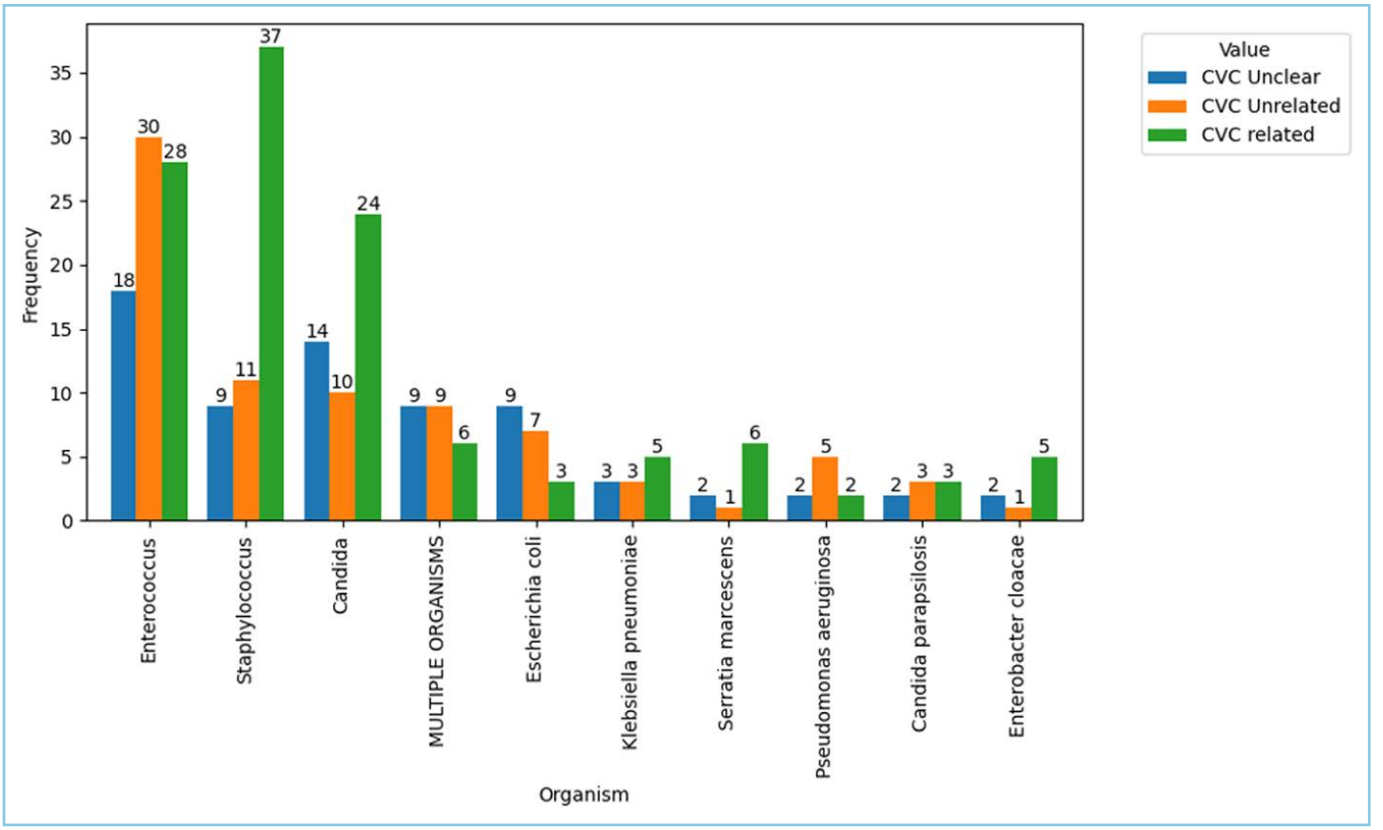

Figure 3. Association of central line-associated bloodstream infection events with cultured organisms. CVC = central venous catheter.

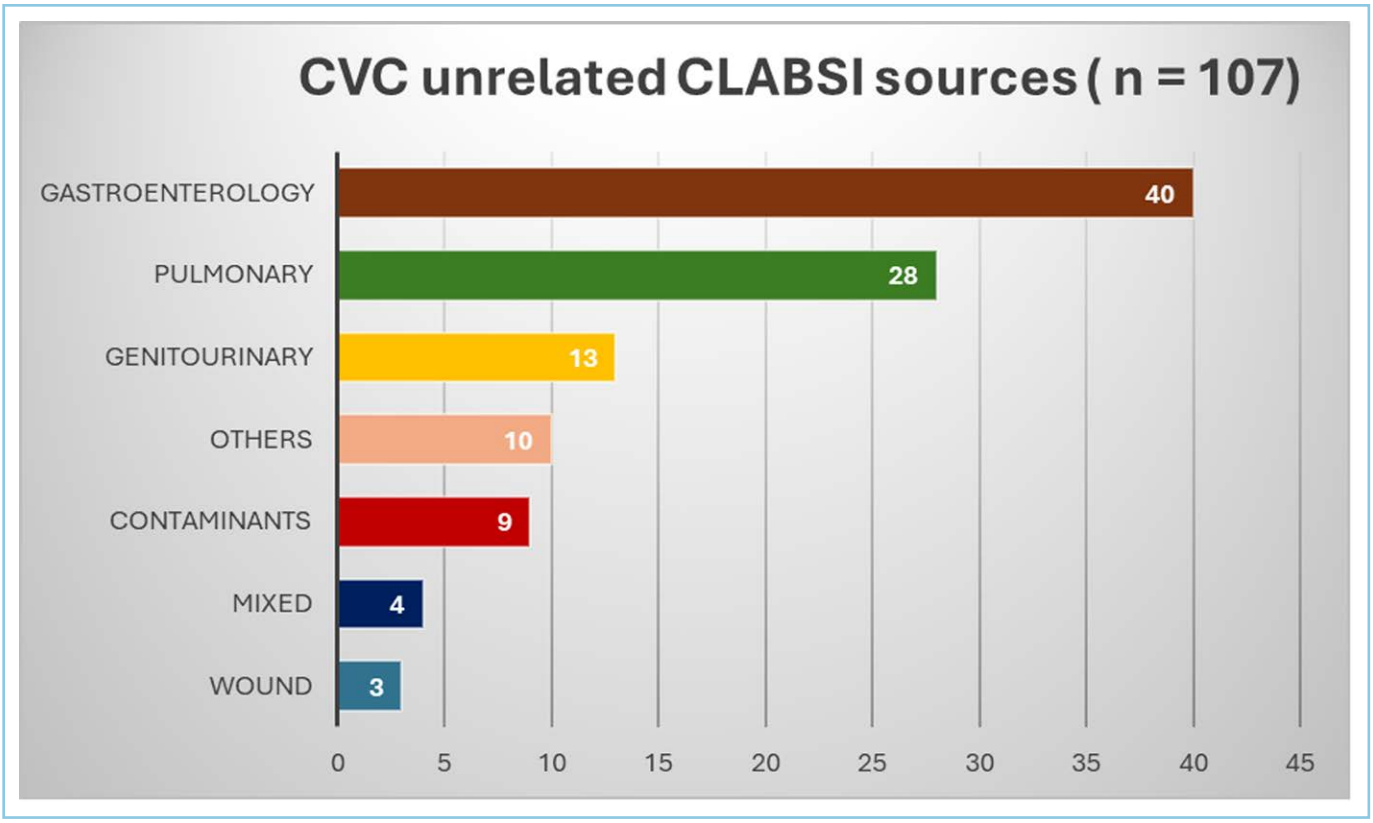

Figure 4. Secondary sources of central venous catheter (CVC)-unrelated central line-associated bloodstream infection (CLABSI) events.

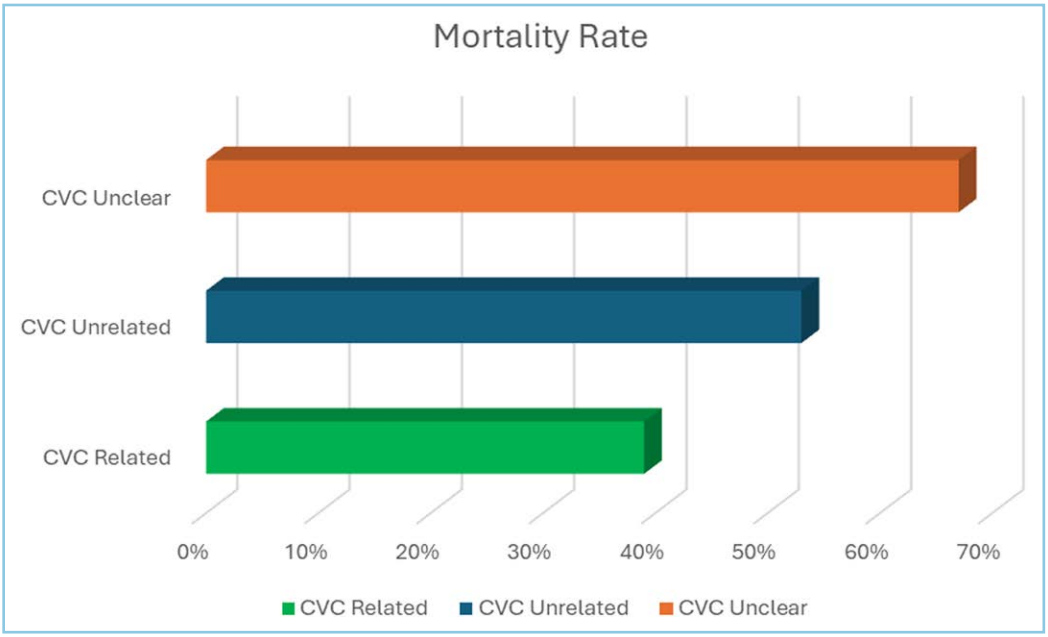

Figure 5. Mortality as an outcome of central line-associated bloodstream infection events in relationship with source. CVC = central venous catheter.

preventive strategies. In our study, focused on VBP ICUs, 31.5% of cases initially classified as CLABSI were attributed to be caused by another infectious source, especially gastrointestinal, pulmonary, and urinary, with *Enterococcus* being the most prevalent bacteria in this group. This suggests that the current CLABSI definition may not be precise enough. *Enterococcus* species and *Candida* species have historically been at the top of the list of our CLABSI pathogens. These are organisms in which the definitions allow very little opportunity for secondary sourcing. It is also important to note that the microbial spectrum might evolve over time. As noted in a surveillance study, there was a decrease of *Staphylococcus* and *Candida*-related infections over time while *Enterococcus* or Gram-negative

organisms related infections remained the same (17). Although, in this study, CRBSI was studied, it is possible that the tenacious nature of the *Enterococcal* and Gram-negative microbiome represents more of secondary seeding and sources of CRBSI (9).

In addition, CLABSIs from CVC-unrelated sources also had higher mortality when compared with CVC related. As postulated, the CVC-related infections might be easier to treat leading to better outcomes compared with other sources. Especially, when the source of infection is unclear to the experts, source control is likely to be harder despite delivery of broad-spectrum antibiotics and could lead to worse outcomes as seen in our CVC-unclear group. Systematic reviews and prevention approaches in these patients cannot be limited to adherence toward application of CLABSI bundles alone. Alternative ID quality measures such as hospital-onset bacteremia and fungemia (HOB) have been proposed; however, the proportion of HOB cases that are preventable remains in question (18, 19).

With the change in prevalence of CLABSI, prior opinions, our study using expert clinician impressions of the source of infection, and the use of CRBSI definition, all have similar results for decreased PPV of the CLABSI definition in relationship with CRBSI (5, 6, 8, 12, 17, 20–22). While CVC insertion and care bundles need to be adhered to, changes in definition and focus on CVC-unrelated CLABSI have the potential to decrease BSIs and improve patient outcomes without penalizing the hospitals. While the significant focus on CLABSI as a quality metric needs to be maintained, the definition itself should be reviewed and possibly revised. This has been done for many quality metrics including the CLABSI definitions itself, as based on Goodhart's law," When a measure becomes a target, it ceases to be a good measure" (23). Metrics, including adherence to bundled metrics for the prevention of CLABSI, might be adequate for the prevention of CVC-related CLABSI, which are already more universally in use. Our analysis also shows that at least at our institution, most of the CLABSIs occur in high acuity, complex care patients admitted to various ICUs. Thus, publication of the CLABSI data should also be reconsidered as the reputational harm for institutions caring for high acuity patients is significant, potentially driving down reimbursement even further than the quality metric associated penalties.

A key limitation of this study is being a single-center, tertiary level institution-based analysis. In the future, a multicenter study could be designed. Another limitation of this analysis is the lack of verifiable laboratory standards such as CVC tip culture results. These are not routinely performed at our institution for CLABSI events. The reason for using ID experts' impression about the source of infection as opposed to other methods, such as CVC tip cultures, was to have an expert's clinically applicable method to describe the source of infection. A similar approach in the past using ID fellow had also found gaps in the utility of CLABSI definition, overestimating CLABSI by 30% (5). These descriptions are important as they drive investigations and treatments of the CLABSI in day-to-day clinical scenarios. These expert clinicians also consider many more factors and investigation results than isolated test results including catheter tip cultures in clinical diagnosis and treatment plans. The results of our study do match prior studies that have used catheter tip culture results. We are also retrospectively assessing and interpreting the documentation of the ID physician's note in this analysis, rather than prospectively assessing the event in possibly a blinded way.

CONCLUSIONS

The definition of CLABSI as a surrogate for CRBSI is inadequate, with a PPV of 58.0% (43.1–67.6%). Efforts should be redirected toward revising the CLABSI definition and possibly reevaluating its criteria. Resources should be assigned to further investigate and systematically prevent BSIs from secondary sources while adhering to existing CLABSI prevention bundles.

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REFERENCES

1. National Healthcare Safety Network: Bloodstream Infection Event (Central Line-Associated Bloodstream Infection and Non-Central Line Associated Bloodstream Infection). 2024. Available at: https://www.cdc.gov/nhsn/psc/bsi/index.html. Accessed June 1, 2024
2. Hallam C, Jackson T, Rajgopal A, et al: Establishing catheter-related bloodstream infection surveillance to drive improvement. *J Infect Prev* 2018; 19:160–166
3. The Joint Commission: Preventing Central Line–Associated Bloodstream Infections: A Global Challenge, a Global Perspective. 2012. Available at: https://psnet.ahrq.gov/issue/preventing-central-line-associated-bloodstream-infections-global-challenge-global-perspective. Accessed June 12, 2024
4. Agency for Healthcare Research and Quality: Toolkit for Reducing Central Line-Associated Blood Stream Infections. 2023. Available at: https://www.ahrq.gov/hai/clabsi-tools/index.html. Accessed June 12, 2024
5. Sopirala MM, Estelle CD, Houston L: Central line-associated bloodstream infection misclassifications-rethinking the Centers for Disease Control and Prevention's central line-associated bloodstream infection definition and its implications. *Crit Care Med* 2024; 52:357–361
6. de Grooth HJ, Timsit JF, Mermel L, et al; 3SITES, CLEAN and DRESSING groups: Validity of surrogate endpoints assessing central venous catheter-related infection: Evidence from individual- and study-level analyses. *Clin Microbiol Infect* 2020; 26:563–571
7. Epstein L, See I, Edwards JR, et al: Mucosal Barrier Injury Laboratory-Confirmed Bloodstream Infections (MBI-LCBI): Descriptive analysis of data reported to National Healthcare Safety Network (NHSN), 2013. *Infect Control Hosp Epidemiol* 2016; 37:2–7
8. Al Hammadi A, Ostrosky-Zeichner L, Boston K, et al: 113. Accuracy of the NHSN Central Line-Associated Bloodstream Infection (CLABSI) definition. *Open Forum Infect Dis* 2018; 5(Suppl 1):S3
9. Bell T, O'Grady NP: Prevention of central line-associated bloodstream infections. *Infect Dis Clin North Am* 2017; 31:551–559
10. Park JY, Kwon KT, Lee WK, et al: The impact of infection control cost reimbursement policy on central line-associated bloodstream infections. *Am J Infect Control* 2020; 48:560–565
11. Centers for Medicare & Medicaid Services: Hospital Value-Based Purchasing Program. 2023. Available at: https://www.cms.gov/medicare/quality/value-based-programs/hospital-purchasing. Accessed June 12, 2024
12. Chen X-X, Lo Y-C, Su L-H, et al: Investigation of the case numbers of catheter-related bloodstream infection overestimated by the central line-associated bloodstream infection surveillance definition. *J Microbiol Immunol Infect* 2015; 48:625–631
13. Odada D, Munyi H, Gatuiku J, et al: Reducing the rate of central line-associated bloodstream infections; a quality improvement project. *BMC Infect Dis* 2023; 23:745
14. Marang-van de Mheen PJ, van Bodegom-Vos L: Meta-analysis of the central line bundle for preventing catheter-related infections: A case study in appraising the evidence in quality improvement. *BMJ Qual Saf* 2016; 25:118–129
15. Gupta P, Thomas M, Patel A, et al: Bundle approach used to achieve zero central line-associated bloodstream infections in an adult coronary intensive care unit. *BMJ Open Qual* 2021; 10:e001200
16. O'Grady NP: Prevention of central line-associated bloodstream infections. *N Engl J Med* 2023; 389:1121–1131
17. Buetti N, Lo Priore E, Atkinson A, et al; Swiss Centre for Antibiotic Resistance (ANRESIS): Catheter-related infections: Does the spectrum of microbial causes change over time? A nationwide surveillance study. *BMJ Open* 2018; 8:e023824
18. Rock C, Thom KA, Harris AD, et al: A multicenter longitudinal study of hospital-onset bacteremia: Time for a new quality outcome measure? *Infect Control Hosp Epidemiol* 2016; 37:143–148
19. Howard-Anderson J, Morgan DJ: Moving beyond central line-associated bloodstream infections. *Ann Intern Med* 2024; 177:822–823
20. Seidelman JL, Kalu IC, Lewis SS, et al: Central-line-associated bloodstream infections secondary to anaerobes: Time for a definition change? *Infect Control Hosp Epidemiol* 2023; 44:1697–1698
21. Hsueh L, de St Maurice A, Uslan DZ: Utilizing new subdefinitions to improve the identification of preventable central-line-associated bloodstream infections (CLABSIs). *Infect Control Hosp Epidemiol* 2023; 44:523–524
22. Sexton DJ, Chen LF, Anderson DJ: Current definitions of central line-associated bloodstream infection: Is the emperor wearing clothes? *Infect Control Hosp Epidemiol* 2010; 31:1286–1289
23. Lamba I: Losing the numbers game: Revisiting quality metrics through the spectrum of Goodhart's law. *Eur J Emerg Med* 2021; 28:176–177