

Archives of Medical Microbiology

Research Article

Predictors of infection clearance rate in intensive care unit patients with catheter-related bloodstream infection

Patel A^{1*}, Reddy A² and Nair K³

¹Division of Clinical Bacteriology, Seine Research Center for Medical Microbiology, Pakistan

²Department of Medical Microbiology, Murray Research Center for Medical Microbiology, Sri Lanka

³Division of Clinical Bacteriology, Fraser Academy of Medical Microbiology, Pakistan

*Address for Correspondence: Arjun Patel, Division of Clinical Bacteriology, Seine Research Center for Medical Microbiology, Pakistan; E-mail: arjun.patel@seine.edu

Received: 16 August 2025; Accepted: 7 November 2025; Published: 9 February 2026.

Citation of this article: Patel A, Reddy A, Nair K (2026) Predictors of infection clearance rate in intensive care unit patients with catheter-related bloodstream infection. Arch Med Microbiol, 8(1): 01-06. DOI: [10.5281/zenodo.22812897](https://doi.org/10.5281/zenodo.22812897)

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Abstract

Background: Catheter-related bloodstream infection (CRBSI) is a major preventable cause of morbidity and mortality in intensive care unit (ICU) patients, and clinicians must decide rapidly whether to remove or attempt to salvage an infected catheter [6,1].

Objective: This study aimed to identify independent clinical, microbiological, and catheter-management predictors of seven-day microbiological clearance in ICU patients with CRBSI.

Methods: We performed a retrospective cohort study of 198 CRBSI episodes in 187 ICU patients at a tertiary referral center over five years, defining clearance as two consecutive negative blood cultures within seven days of appropriate therapy, and analyzed predictors using multivariable logistic regression.

Results: Overall, 66.7% of episodes cleared within seven days. Catheter removal within 24 hours (adjusted OR 3.42), coagulase-negative staphylococcal infection (aOR 2.61), timely appropriate empiric therapy (aOR 2.35), and absence of septic shock (aOR 2.18) independently predicted clearance, while Candida infection (aOR 0.44) and immunosuppression (aOR 0.48) independently predicted failure to clear [10,12].

Conclusions: Prompt catheter removal, causative organism, timely appropriate therapy, and illness severity independently determine clearance rate in ICU-associated CRBSI, supporting organism-informed, early source-control decision-making [13,9].

Keywords: catheter-related bloodstream infection; intensive care unit; microbiological clearance; catheter removal; predictors

1. Introduction

Catheter-related bloodstream infection (CRBSI) remains one of the most consequential preventable complications of intensive care, contributing directly to attributable mortality, prolonged mechanical ventilation, and extended intensive care unit (ICU) stay [1,2]. Large multinational surveillance efforts have repeatedly identified central venous catheters as the leading device-associated source of nosocomial bloodstream infection, with organism distribution dominated by coagulase-negative staphylococci, *Staphylococcus aureus*, enteric gram-negative bacilli, and, increasingly in critically ill and immunosuppressed cohorts, *Candida* species [3,4,5]. Clinicians managing an ICU patient with a newly diagnosed CRBSI face an immediate decision: whether to remove the catheter promptly, attempt salvage with systemic antibiotics with or without an antibiotic lock, and how aggressively to pursue source control when vascular access is difficult to replace [6,7].

The rate at which bloodstream infection clears following diagnosis, rather than simple survival to discharge, is a clinically meaningful intermediate outcome because it is proximate to the interventions clinicians actually control and captures treatment failure earlier than mortality alone [8,9]. Time to clearance is influenced by a heterogeneous set of factors spanning the causative organism's biofilm-forming capacity, the timing of catheter removal, the adequacy and timing of empiric antimicrobial therapy, and host factors such as immunosuppression and severity of illness at diagnosis [10,11,12]. Randomized data on watchful waiting versus immediate catheter removal in ICU patients with suspected catheter infection suggest that deferring removal is feasible in selected low-risk patients, but the trial was not powered to resolve which host and microbiological features predict a fast versus a protracted clearance trajectory once bacteremia is confirmed [13].

Retrospective cohorts examining catheter-related

bacteremia in critically ill patients have consistently identified organism virulence, particularly *Staphylococcus aureus* and *Candida* species, as associated with slower clearance and higher attributable mortality relative to coagulase-negative staphylococci [14,15,16], while delayed catheter removal, prolonged catheter dwell time, and structured prevention bundles have been examined chiefly as determinants of infection incidence rather than of the clearance trajectory once infection has already occurred [17,18,19,20,21,22,23]. Comparatively few ICU studies have modeled clearance rate as the primary endpoint in a multivariable framework accounting simultaneously for organism type, catheter management, and baseline severity of illness.

This study was undertaken to identify independent clinical, microbiological, and management-related predictors of infection clearance rate among ICU patients diagnosed with CRBSI at a tertiary referral center, with the goal of informing bedside decisions about catheter salvage versus removal and the intensity of source-control efforts.

2. Methods

Study design and setting

We conducted a retrospective cohort study of adult patients admitted to the general and surgical intensive care units of a tertiary referral hospital who developed a microbiologically confirmed catheter-related bloodstream infection over a five-year period. The study was approved by the institutional ethics review board, and the requirement for individual informed consent was waived given the retrospective, de-identified nature of the analysis.

Case definition and identification

CRBSI was defined according to the Infectious Diseases Society of America clinical practice guideline criteria, requiring at least one positive peripheral blood culture, clinical manifestations of bloodstream infection with no other apparent source, and microbiological confirmation

of catheter involvement by either differential time to positivity of paired hub and peripheral cultures exceeding two hours, quantitative catheter-tip culture growth exceeding 15 colony-forming units, or concordant organism growth from catheter-tip and peripheral cultures [6,24]. Cases were identified through prospective infection-control surveillance records cross-checked against the clinical microbiology laboratory database, and each case was independently reviewed by two investigators to confirm eligibility.

Data collection

For each eligible patient we abstracted demographics, admission diagnosis, APACHE II and SOFA scores at CRBSI diagnosis, comorbidities (diabetes, chronic kidney disease, malignancy), immunosuppressive status (neutropenia, corticosteroids exceeding 20 mg prednisone-equivalent daily for over two weeks, or cytotoxic chemotherapy within 30 days), catheter type, insertion site and dwell time, causative organism and susceptibility profile, timing/adequacy of empiric therapy, timing of catheter removal, use of antibiotic lock salvage, and presence of septic shock at diagnosis.

Outcome definition

The primary outcome, infection clearance rate, was defined as the proportion of patients achieving microbiological clearance, confirmed by two consecutive negative blood cultures drawn at least 24 hours apart, within seven days of appropriate antimicrobial therapy initiation. Time to clearance in days was recorded as a secondary, continuous representation of the same endpoint. Patients who died before clearance could be documented, or who were transferred to another facility within seven days, were classified as not having achieved clearance for the primary analysis, consistent with the approach used in prior catheter-related bacteremia outcome studies [8,15].

Statistical analysis

Categorical variables were compared using chi-square or

Fisher's exact test; continuous variables were compared using Student's t-test or Mann-Whitney U test according to distribution. Variables associated with clearance at $p < 0.10$ univariably, plus variables of established clinical relevance, were entered into a multivariable logistic regression model with seven-day clearance as the dependent variable, reported as adjusted odds ratios (aOR) with 95% confidence intervals. Time-to-clearance was examined by Kaplan-Meier estimation with log-rank comparison. A two-sided $p < 0.05$ was considered significant.

3. Results

Cohort characteristics

Over the five-year study period, 214 episodes of CRBSI meeting the case definition were identified, of which 198 episodes in 187 unique patients had complete data and were retained. Median age was 61 years (IQR 48-72), and 58.6% were male. Median APACHE II score at diagnosis was 22 (IQR 17-27), and 41.4% had septic shock at diagnosis. Central venous catheters accounted for 71.2% of infected devices, followed by hemodialysis catheters (16.7%) and peripherally inserted central catheters (12.1%); the femoral site carried the highest crude infection density, consistent with prior comparative series [18,17].

Causative organisms and clearance rate

Coagulase-negative staphylococci were the most common isolate (34.3%), followed by *Staphylococcus aureus* (23.7%, of which 46.8% were methicillin-resistant), *Candida* species (17.2%), and gram-negative bacilli including *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa* (24.8%). Overall, 132 of 198 episodes (66.7%) achieved microbiological clearance within seven days. Clearance rates differed substantially by organism: 82.4% for coagulase-negative staphylococci, 68.1% for gram-negative bacilli, 51.1% for *Staphylococcus aureus*, and 41.2% for *Candida* species ($p < 0.001$), a pattern consistent with the comparatively slower clearance

previously reported for *S. aureus* and *Candida* catheter infections in critically ill cohorts [14,16].

Table 1: Baseline characteristics of 198 catheter-related bloodstream infection episodes by seven-day clearance status [12,15].			
Characteristic	Cleared (n=132)	Not cleared (n=66)	p-value
Median age, years (IQR)	59 (46-70)	65 (52-75)	0.041
Male sex, %	56.8	62.1	0.46
Median APACHE II (IQR)	20 (16-25)	26 (21-30)	<0.001
Septic shock at diagnosis, %	31.8	60.6	<0.001
Immunosuppressed, %	21.2	39.4	0.007
Catheter removed <24h, %	72.0	39.4	<0.001

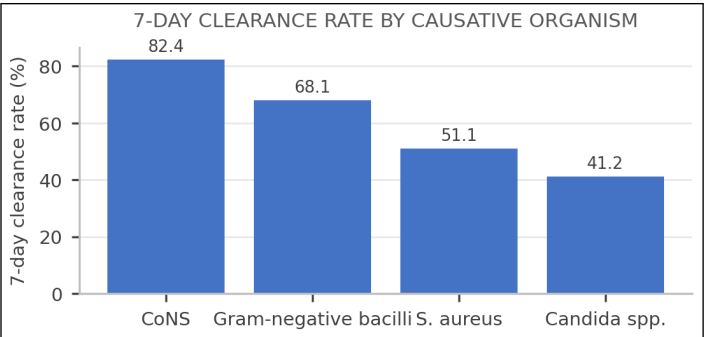


Figure 1: Seven-day microbiological clearance rate by causative organism among 198 episodes of catheter-related bloodstream infection, highest for coagulase-negative staphylococci and lowest for *Candida* species [14,16].

Catheter management and clearance

Catheter removal within 24 hours of diagnosis was performed in 61.1% of episodes and was associated with a substantially higher clearance rate than delayed removal beyond 24 hours or catheter salvage with antibiotic lock therapy alone (78.5% versus 49.4%, $p<0.001$). Among the 38 episodes managed with catheter salvage and antibiotic lock therapy, clearance was achieved in 55.3%, a rate intermediate between prompt removal and delayed removal without lock therapy, broadly in line with prior salvage-therapy experience [7,25]. Median time to clearance among all patients who cleared infection was 3 days (interquartile range 2-5), and Kaplan-Meier estimation showed significantly faster clearance with early

catheter removal (log-rank $p<0.001$) and with coagulase-negative staphylococcal infection relative to *S. aureus* or *Candida* infection (log-rank $p<0.001$).

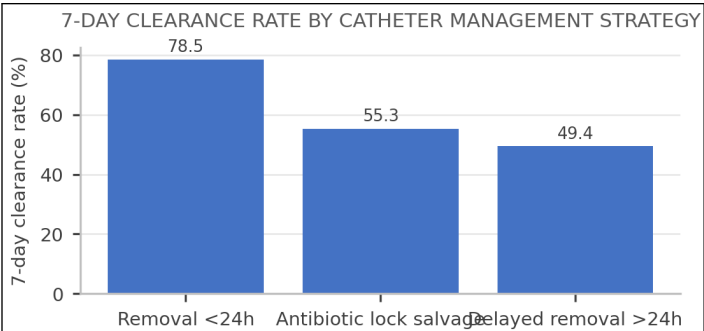


Figure 2: Seven-day clearance rate by catheter management strategy, showing the highest clearance with catheter removal within 24 hours of diagnosis and the lowest with delayed removal beyond 24 hours [13,7].

Predictors of clearance in multivariable analysis

On multivariable logistic regression, four factors were independently associated with seven-day clearance: catheter removal within 24 hours of diagnosis (aOR 3.42, 95% CI 1.78-6.58, $p<0.001$), infection with coagulase-negative staphylococci relative to other organisms (aOR 2.61, 95% CI 1.31-5.19, $p=0.006$), appropriate empiric antimicrobial therapy initiated within 24 hours (aOR 2.35, 95% CI 1.19-4.64, $p=0.014$), and absence of septic shock at diagnosis (aOR 2.18, 95% CI 1.10-4.31, $p=0.025$). *Candida* infection (aOR 0.44, 95% CI 0.20-0.96, $p=0.038$) and immunosuppressed status (aOR 0.48, 95% CI 0.23-0.99, $p=0.046$) were independently associated with lower odds of clearance. Catheter dwell time before infection, APACHE II score as a continuous variable, and diabetes mellitus were not independently associated with clearance after adjustment. These findings are summarized in the multivariable model presented in Table 2 and are consistent with the pattern reported by prior studies modeling predictors of clinical response in catheter-related bacteremia [8,12].

Table 2: Independent predictors of seven-day microbiological clearance on multivariable logistic regression [8].

Predictor	Adjusted OR	95% CI	p-value
Catheter removal <24h	3.42	1.78-6.58	<0.001
Coagulase-negative staphylococci	2.61	1.31-5.19	0.006
Timely appropriate empiric therapy	2.35	1.19-4.64	0.014
Absence of septic shock	2.18	1.10-4.31	0.025
Immunosuppression	0.48	0.23-0.99	0.046
Candida infection	0.44	0.20-0.96	0.038

Mortality and secondary outcomes

Twenty-eight-day all-cause mortality was 18.7% among patients who achieved seven-day clearance versus 43.9% among those who did not ($p < 0.001$), a gradient consistent with the attributable mortality previously described for catheter-related bloodstream infection in meta-analyses of critically ill cohorts [9,26]. ICU length of stay was also significantly shorter among patients who cleared infection within seven days (median 9 versus 15 days, $p < 0.001$).

4. Discussion

In this cohort of ICU patients with catheter-related bloodstream infection, roughly two-thirds of episodes achieved microbiological clearance within seven days, and clearance was independently predicted by prompt catheter removal, causative organism, timely appropriate empiric therapy, and absence of septic shock at diagnosis. These findings are broadly concordant with the existing catheter-infection literature while extending it by modeling clearance rate, rather than mortality alone, as the primary multivariable endpoint in a contemporary ICU population.

The strong independent association between catheter removal within 24 hours and clearance reinforces the central recommendation of current guideline documents, which prioritize source control as the single most actionable intervention once CRBSI is diagnosed [6,27]. This finding also adds granularity to the randomized comparison of watchful waiting against immediate removal reported by Rijnders and colleagues, which

showed deferred removal could be safe in carefully selected low-risk patients but left open which patients tolerate delay without a meaningfully worse clearance trajectory [13]. Organism identity appears to be one plausible discriminator: episodes caused by coagulase-negative staphylococci, which are less virulent and less prone to biofilm-mediated catheter persistence than *S. aureus*, cleared substantially faster and may represent the population in whom a trial of catheter salvage is most defensible [10,11].

Conversely, the markedly lower clearance rate observed with *Staphylococcus aureus* and *Candida* infection reproduces a consistent theme across the catheter-infection literature: both organisms form robust, antimicrobial-tolerant biofilms on intraluminal catheter surfaces, and clearance in the presence of a retained infected device is correspondingly less likely regardless of systemic antimicrobial adequacy [28,16,8]. This mechanistic link argues against prolonged salvage attempts with antibiotic lock therapy for these organisms outside carefully selected patients with severely limited vascular access, consistent with the more modest role for lock therapy suggested in prior meta-analyses restricted largely to less virulent organisms [25,7].

The independent association between septic shock at diagnosis and lower odds of clearance likely reflects both greater bacterial burden and impaired host clearance mechanisms in the most physiologically deranged patients, a pattern also described in cohort studies linking illness severity to catheter-related bacteremia outcomes [12,15]. Similarly, the adverse association with immunosuppression is consistent with the well-documented vulnerability of neutropenic and corticosteroid-treated patients to prolonged catheter-associated bacteremia, in whom earlier and more aggressive source control has been specifically recommended [29]. That timely appropriate empiric therapy independently predicted clearance even after

adjustment for organism and catheter management underscores the importance of local resistance surveillance and rapid diagnostics, given the substantial proportion of methicillin-resistant *S. aureus* observed here [3,30].

These results complement, rather than substitute for, the substantial preventive literature showing that insertion-related interventions such as maximal sterile barrier precautions, chlorhexidine-based antisepsis, and chlorhexidine-impregnated dressings reduce CRBSI incidence before it ever occurs [21,22,23,31,20]: even in units with low incidence through bundled prevention, a minority of infections will still occur, and the present data offer a framework for triaging salvage versus removal once infection has developed. The higher 28-day mortality observed among patients who did not clear infection within seven days is consistent with prior meta-analytic estimates of attributable mortality for CRBSI in critically ill populations and supports clearance rate as a clinically actionable intermediate outcome [9,26,2].

This study has several limitations. As a retrospective single-center cohort, residual confounding by indication cannot be excluded, particularly in the decision to attempt catheter salvage rather than immediate removal, which likely reflects clinician judgment about vascular access difficulty and perceived severity. The modest sample size limits precision for less common organism subgroups, and larger multicenter cohorts would allow more granular modeling. Finally, clearance was defined using a fixed seven-day window; some patients who did not meet this threshold may have cleared subsequently with continued therapy, which would tend to underestimate the true eventual clearance rate.

5. Conclusion

Among ICU patients with catheter-related bloodstream infection, prompt catheter removal within 24 hours, infection with coagulase-negative staphylococci, timely appropriate empiric antimicrobial therapy, and absence

of septic shock at diagnosis were independently associated with higher rates of seven-day microbiological clearance, while *Candida* infection and immunosuppression were independently associated with lower clearance. These findings support early, organism-informed decision-making about catheter removal versus salvage in this population and reinforce clearance rate as a clinically actionable early outcome that complements the substantial existing literature on CRBSI prevention.

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