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Heparin-Coated Catheters and Reduction of Catheter-Related Bloodstream Infection in Sepsis Patients

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ABSTRACT

Background: Central venous catheters are essential to the resuscitation and monitoring of sepsis and septic shock, but the same indwelling device is a leading modifiable source of catheter-related bloodstream infection (CRBSI), a risk compounded in septic patients by prolonged dwell time and sepsis-associated coagulopathy that links catheter thrombosis mechanistically to catheter infection. Objective: This narrative review synthesizes the published evidence on heparin-coated and heparin-bonded central venous and related catheters as a strategy for reducing CRBSI and catheter thrombosis, with particular attention to critically ill and sepsis-adjacent populations. Methods: Peer-reviewed randomized trials, comparative cohort studies, and Cochrane systematic reviews addressing heparin-coated or heparin-bonded catheters, alongside foundational sepsis, catheter-infection epidemiology, and guideline literature, were identified and synthesized thematically around pathophysiological rationale, adult and critically ill trial evidence, pediatric and systematic review evidence, hemodialysis-catheter evidence, and implementation context. Findings: Heparin coating reduces CRBSI relative to uncoated catheters, with a randomized hematology-oncology trial reporting infection rates of 2.5% versus 9.1% (0.9 versus 3.5 episodes per 1,000 catheter-days) and a pooled pediatric Cochrane analysis reporting a number needed to treat of 6 to prevent one CRBSI event and 13 to prevent one catheter occlusion event. Against newer antiseptic- and antibiotic-impregnated catheters, however, heparin-coated devices have shown an inconsistent or unfavorable comparative advantage in general critically ill and pediatric populations, and heparin coating's infection benefit and thrombosis benefit appear to dissociate in some catheter types, including tunneled hemodialysis catheters. Conclusions: Heparin-coated catheters are a mechanistically coherent and evidence-supported, but not uniformly superior, adjunct to bundle-based CRBSI prevention in sepsis; their comparative role relative to antiseptic-impregnated catheters, and their specific benefit in coagulopathic, thrombosis-prone septic patients, warrants dedicated prospective evaluation.

Keywords: *heparin-coated catheter; catheter-related bloodstream infection; central venous catheter; sepsis; catheter thrombosis prevention*

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Introduction

Central venous catheters are indispensable in the management of sepsis and septic shock, providing the vascular access required for rapid fluid resuscitation, vasopressor delivery, and hemodynamic monitoring that define modern critical care [1]. Yet the same indwelling device that makes early, aggressive sepsis management possible is itself a major, modifiable driver of subsequent nosocomial bloodstream infection: multinational point-prevalence data from more than 1,200 intensive care units found that 51% of patients were considered infected on the day of assessment, with the respiratory and abdominal sources predominating but catheter-related bloodstream infection (CRBSI) remaining one of the most consistently identified and preventable secondary infections acquired after intensive care unit admission [2]. Because sepsis patients already carry deranged coagulation, impaired innate immunity, and prolonged catheter dwell times, they are disproportionately exposed to the biological process that links an indwelling catheter to bloodstream infection: extraluminal and intraluminal deposition of a fibrin sheath and biofilm on the catheter surface, which not only shelters adherent organisms from host defenses and systemic antibiotics but also mechanically predisposes to catheter thrombosis, creating a self-reinforcing cycle in which thrombosis promotes infection and infection promotes further thrombogenicity [3,4].

This mechanistic coupling of thrombosis and infection has motivated more than four decades of research into catheter surface modification as an infection-prevention strategy, of which heparin bonding or coating was among the earliest approaches tested, predating the antiseptic- and antibiotic-impregnated catheters that now dominate clinical guidelines [5]. Heparin was first adopted for its anticoagulant, anti-thrombogenic property, intended to prevent catheter occlusion and central venous thrombosis rather than to prevent infection directly, but subsequent laboratory and clinical work identified two additional properties relevant to this narrative review's focus: heparin's capacity to reduce microbial adherence to catheter polymer surfaces, and its capacity to reduce the fibrin substrate onto which bacteria and fungi preferentially adhere and form biofilm, providing a biologically plausible pathway by which heparin coating could reduce CRBSI incidence independent of, or in addition to, any purely antimicrobial mechanism [3]. Because sepsis and septic shock are the clinical settings in which catheter dwell time, catheter number, and baseline coagulopathy are all simultaneously maximized, they represent the population in which a catheter-surface intervention targeting the thrombosis-infection axis should, in principle, deliver its greatest benefit.

This narrative review synthesizes the published literature on heparin-coated and heparin-bonded central venous and related catheters around five themes: the pathophysiological rationale linking catheter thrombogenicity to bloodstream infection; the randomized trial evidence comparing heparin-coated catheters against uncoated and antiseptic-coated alternatives in adults; the pediatric and Cochrane systematic review evidence, which provides the most rigorously pooled quantitative estimates available; extension of the heparin-coating concept to hemodialysis and other specialized catheters relevant to the septic patient with acute kidney injury; and the comparative limitations and next-generation coatings that shape heparin coating's place in a modern CRBSI-prevention strategy for sepsis.

Pathophysiological Rationale: The Thrombosis-Infection Axis

Within seconds to minutes of insertion, any intravascular catheter is coated by host plasma proteins, including fibrinogen, fibronectin, and von Willebrand factor, forming a conditioning film that both promotes platelet and fibrin deposition and provides adhesion receptors for staphylococcal and other bacterial surface proteins [3]. This fibrin sheath, which develops on most central venous catheters left in place beyond five to seven days, functions as an extraluminal reservoir in which organisms migrating from the insertion site or seeding hematogenously can embed and organize into a protected biofilm matrix substantially more resistant to systemic antimicrobial therapy and host phagocytic clearance than planktonic organisms in blood [4]. The corollary is that catheter-related venous thrombosis and CRBSI are not independent complications but correlated events: risk factors that promote one, prolonged dwell time, subclavian or femoral insertion site, multiple lumens, and the hypercoagulable, endothelium-injured state of sepsis itself, tend to promote the other, creating the rationale for an intervention aimed at the shared thrombogenic substrate [3,5].

Guideline bodies have long recognized this coupling in their evidence grading. The Infectious Diseases Society of America's guidelines for the management of intravascular catheter-related infections discuss the contribution of catheter-associated thrombus to refractory or relapsing bacteremia and fungemia, particularly in septic thrombophlebitis, noting that anticoagulation or thrombus-reducing strategies may be adjunctive considerations in selected catheter infections with associated thrombosis [4]. The Centers for Disease Control and Prevention's guidelines for the prevention of intravascular catheter-related infections similarly catalog antimicrobial- and antiseptic-impregnated catheters as a category of technology-based prevention, of which heparin-coated devices represent a chemically and historically distinct branch predating chlorhexidine-silver sulfadiazine and minocycline-rifampin surface technologies by more than a decade [5].

Chronology and mechanistic basis of catheter coating technologies discussed in this review.

Coating technology	Primary mechanism	Representative reference
Heparin bonding/coating	Reduces fibrin sheath deposition and surface thrombogenicity; electrostatic and anti-adhesive reduction of bacterial attachment	Maki et al. 2006; Pierce et al. 2000
Chlorhexidine-silver sulfadiazine (first- and second-generation)	Broad-spectrum antiseptic surface activity	Darouiche et al. 1999; Carrasco et al. 2004
Minocycline-rifampin	Antibiotic surface elution	Darouiche et al. 1999
Heparin-network multifunctional coating	Combined durable antithrombotic and antibacterial surface activity	Liu et al. 2024

Laboratory work has shown that heparin bonding reduces in vitro adherence of coagulase-negative staphylococci and other common catheter pathogens to polymer surfaces, an effect attributed both to heparin's net negative surface charge, electrostatically repulsive to many bacterial surface structures, and to its capacity to limit deposition of the fibrinogen- and fibronectin-rich conditioning film that would otherwise serve as an adhesion substrate [3]. Contemporary materials-science work has extended this picture considerably: a heparin-network coating chemistry combining heparin sodium with an organosilicon quaternary ammonium surfactant conferred simultaneous, durable antithrombotic and antibacterial activity on intravascular catheter surfaces in vivo, demonstrating that a single heparin-based coating can be engineered to address both arms of the thrombosis-infection axis, and bridging the original heparin-bonded catheters evaluated clinically from the 1980s through 2000s to next-generation multifunctional coatings now in development [6]. Together, this literature establishes a coherent, biologically plausible basis for evaluating heparin coating as a CRBSI-prevention strategy against which the clinical trial evidence below should be interpreted.

Randomized Trial Evidence in Adults and Critically Ill Populations

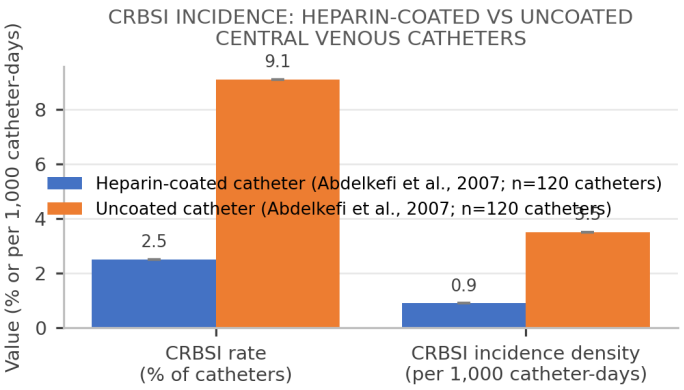
The clinical trial literature testing heparin-coated or heparin-bonded catheters against uncoated or alternatively coated devices spans hematology-oncology, general intensive care, and comparative antiseptic-catheter designs, and it is this body of evidence that bears most directly on the sepsis population targeted by this review. In a prospective, randomized trial conducted in 240 patients with hematologic and oncologic disease

requiring nontunneled central venous catheterization, Abdelkefi and colleagues randomized patients to a heparin-coated catheter or a standard, uncoated catheter and found a CRBSI rate of 2.5% (3 of 120 catheters, 0.9 episodes per 1,000 catheter-days) in the heparin-coated group compared with 9.1% (11 of 120 catheters, 3.5 episodes per 1,000 catheter-days) in the uncoated control group, a statistically significant difference (P = .027) corresponding to a relative risk of 0.27 (95% confidence interval, 0.08-0.95), representing an approximately 73% relative risk reduction in CRBSI with heparin coating [7]. This trial remains among the clearest head-to-head demonstrations that heparin coating alone, without any antiseptic or antibiotic agent, can meaningfully lower CRBSI incidence in a population with substantial catheter-days and baseline infection risk analogous to that of critically ill septic patients.

Principal randomized and comparative trials of heparin-coated or heparin-bonded catheters referenced in this review, by population and comparator.

Study	Population / catheter type	Comparison	Principal finding
Abdelkefi et al. 2007	240 hematology-oncology patients, nontunneled CVC	Heparin-coated vs uncoated	CRBSI 2.5% vs 9.1% (0.9 vs 3.5 per 1,000 catheter-days); RR 0.27 (95% CI 0.08-0.95), P=.027
Carrasco et al. 2004	Medical-surgical ICU patients, triple-lumen CVC	Heparin-coated vs chlorhexidine-silver sulfadiazine coated	Chlorhexidine-silver sulfadiazine catheter associated with lower colonization, particularly gram-positive and fungal
Darouiche et al. 1999	Multicenter adult ICU/hospital patients, CVC	Chlorhexidine-silver sulfadiazine vs minocycline-rifampin coated	Minocycline-rifampin catheter had significantly lower colonization and CRBSI
Gilbert et al. 2016 (CATCH trial)	1,485 children requiring CVC	Antimicrobial-impregnated vs standard polyurethane catheter	Impregnated catheters reduced bloodstream infection risk versus standard catheters
Jain et al. 2009	175 tunneled hemodialysis catheters	Heparin-coated vs noncoated	Heparin coating decreased catheter-related bacteremia; did not reduce catheter malfunction

Catheter-related bloodstream infection (CRBSI) incidence in a randomized trial of heparin-coated versus uncoated nontunneled central venous catheters in 240 hematology-oncology patients, expressed both as the percentage of catheters infected and as episodes per 1,000 catheter-days (Abdelkefi et al., 2007).



By contrast, when heparin-coated catheters have been compared directly against second-generation antiseptic-coated devices rather than against uncoated controls, the comparative advantage of heparin coating has been less consistent. Carrasco and colleagues, in a randomized trial in a 20-bed medical-surgical intensive care unit, compared triple-lumen heparin-coated catheters against catheters coated with chlorhexidine and silver sulfadiazine and found that the chlorhexidine-silver sulfadiazine catheter was associated with lower colonization, particularly by gram-positive organisms and fungi, suggesting that in a general critically ill population an antiseptic coating may outperform a purely anti-thrombogenic coating for colonization outcomes, even though both outperform uncoated devices in the broader literature [8]. This is consistent with the wider antiseptic-catheter literature: Darouiche and colleagues' landmark multicenter comparison of a first-generation chlorhexidine-silver sulfadiazine catheter against a minocycline-rifampin catheter found significantly lower colonization and CRBSI with the minocycline-rifampin device, establishing the comparative benchmark against which any coating technology, heparin included, must be judged in critically ill and immunocompromised populations [9]. This infection-focused literature builds on an older, patency-focused tradition: Randolph and colleagues, pooling randomized trials of heparin used with central venous and pulmonary artery catheters, found that heparin significantly reduced catheter-associated thrombosis, establishing more than two decades ago the anti-thrombotic premise on which the infection-prevention rationale for heparin coating was later built, even though that meta-analysis was not powered to assess CRBSI [10].

Taken together, the adult trial literature supports two conclusions relevant to sepsis. First, heparin coating reduces CRBSI relative to uncoated catheters with a magnitude, in the best-designed available trial, comparable to or exceeding that reported for some antiseptic coatings relative to uncoated devices, supporting heparin coating as a legitimate, mechanistically distinct strategy rather than a historical curiosity [7]. Second, where heparin-coated and antiseptic-coated catheters have been compared head-to-head, the antiseptic-coated catheter has more often shown a colonization advantage, suggesting heparin coating's comparative niche lies less in supplanting antiseptic catheters in unselected critically ill patients and more in settings, discussed below, where thrombosis and infection prevention are both necessary and antiseptic coatings are contraindicated, unavailable, or understudied [8,9].

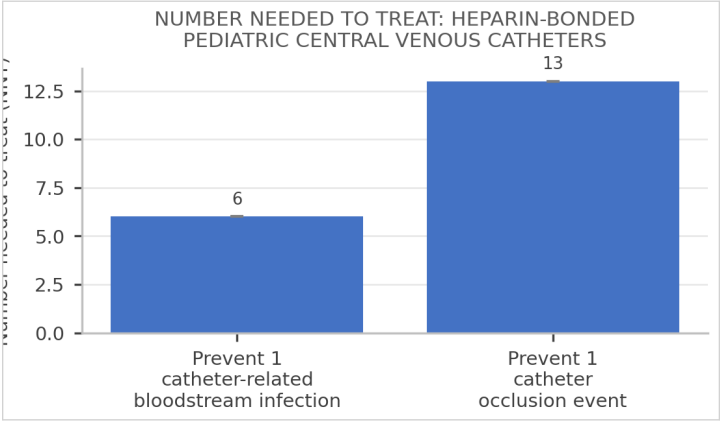
Pediatric and Systematic Review Evidence

The most methodologically rigorous quantitative evidence for heparin-bonded catheters comes from the pediatric literature and its associated Cochrane systematic reviews, which benefit from a comparatively focused trial base and from Cochrane's structured risk-of-bias and pooling methodology. Pierce and colleagues, in a randomized trial conducted among critically ill children requiring central venous access, found that heparin-bonded central venous lines reduced both thrombotic complications and infective complications compared with standard, non-bonded lines, providing one of the first prospective demonstrations that a single coating technology could simultaneously address both halves of the thrombosis-infection axis described above in a pediatric critical care population, a population that shares with septic adults the combination of prolonged catheter dwell time and heightened baseline infection risk [11].

The Cochrane systematic review by Shah and Shah, which pooled the available randomized trials of heparin-bonded catheters for prolonging patency of central venous catheters in children, found that heparin-bonded catheters were associated with a statistically significant reduction in the risk of catheter-related bloodstream infection, with a number needed to treat of 6 (95% confidence interval, 4-10) to prevent one CRBSI event, and a statistically significant reduction in the risk of catheter occlusion, with a number needed to treat of 13 to prevent one occlusion event; the review's authors nonetheless cautioned that these benefits derived from a single included trial and that further well-designed, multicenter randomized trials were needed before heparin bonding could be considered definitively established practice [12]. A number needed to treat of 6 for CRBSI prevention is a clinically substantial effect size by the standards of infection-control interventions, and it is notable that this effect emerged from the same pediatric critical care literature, exemplified by Pierce and colleagues' trial, that first demonstrated heparin bonding's dual thrombosis-infection benefit [11,12].

The companion adult-focused Cochrane review by Lai and colleagues, evaluating catheter impregnation, coating, or bonding for reducing central venous catheter-related infections in adults across antiseptic, antibiotic, and heparin-based approaches, situates heparin coating within this broader technology landscape, concluding that antimicrobial-impregnated catheters as a class reduce CRBSI risk relative to standard catheters while also highlighting substantial heterogeneity across the individual coating technologies pooled, heparin among them [13]. Because this adult review pools heparin coating alongside chemically distinct technologies rather than presenting a heparin-specific pooled estimate, clinicians managing septic patients cannot yet draw on a single, adult-specific, heparin-only effect size in the way pediatric intensivists can draw on the Shah and Shah number-needed-to-treat estimate, a persistent evidence gap later sections address directly [13,12].

Number needed to treat (NNT) with a heparin-bonded central venous catheter, relative to a standard non-bonded catheter, to prevent one catheter-related bloodstream infection event versus one catheter occlusion event, pooled from randomized pediatric trials in the Cochrane review by Shah and Shah (2014).



Complementing these infection-focused reviews, the Cochrane review of heparin versus 0.9% sodium chloride intermittent flushing for catheter patency maintenance, mechanistically related through its shared reliance on heparin exposure but distinct from surface bonding, found no conclusive evidence of an important difference between heparin and saline flushing for preventing catheter occlusion in adults, a null result that contrasts with the positive surface-bonding findings above and suggests heparin's benefit is more consistent when bonded to the catheter surface, continuously exposing the fibrin sheath to a thromboresistant interface, than when administered intermittently as a lock or flush solution [14].

Extension to Hemodialysis and Specialized Catheters in Sepsis-Adjacent Populations

Sepsis and septic shock frequently coexist with acute kidney injury requiring renal replacement therapy, and the hemodialysis catheter literature therefore offers directly relevant, if population-adjacent, evidence on heparin coating's infection-prevention performance in a group of critically ill patients who share the coagulopathy, prolonged catheter dwell time, and heightened infection vulnerability of septic patients. Jain and colleagues compared 89 heparin-coated tunneled dialysis catheters against 86 noncoated catheters and found that heparin coating decreased the frequency of catheter-related bacteremia, though it did not reduce the frequency of catheter malfunction or thrombotic occlusion, an outcome pattern that partially diverges from the pediatric central venous catheter literature, in which heparin bonding reduced both thrombotic and infective complications together, and that suggests the infection-prevention and thrombosis-prevention benefits of heparin coating may dissociate depending on catheter type, insertion site, and dwell duration [15]. Clark and colleagues, in a comparison of heparin-coated and conventional split-tip hemodialysis catheters, similarly examined complication rates between the two catheter designs and contributed further comparative data on device-specific outcomes relevant to interpreting heparin coating's role in the hemodialysis-catheter subset of the critically ill population, reinforcing that catheter design (split-tip versus standard) and coating chemistry interact in ways that single-variable trials of coating alone cannot fully isolate [16].

These hemodialysis-catheter findings carry two implications for sepsis patients specifically. First, they indicate that heparin

coating's bacteremia-reducing effect is not confined to conventional multi-lumen central venous catheters used for fluid and vasopressor administration but extends to the specialized, larger-bore catheters used for continuous or intermittent renal replacement therapy, a device category increasingly common in septic shock complicated by acute kidney injury. Second, the dissociation between infection benefit and thrombosis benefit observed by Jain and colleagues cautions against assuming that heparin coating's mechanism of action, and therefore its expected magnitude of clinical benefit, is uniform across all catheter types and insertion sites; the pediatric non-dialysis central venous catheter literature and the adult hemodialysis catheter literature should therefore be regarded as complementary rather than interchangeable evidence when extrapolating to the specific catheters most commonly placed in adult sepsis patients [15,11].

Implementation Context, Comparative Limitations, and Future Directions

Any discussion of a single catheter-technology intervention for CRBSI prevention in sepsis must be situated within the broader, multi-component infection-prevention framework that has demonstrably reduced CRBSI rates independent of catheter coating choice. Pronovost and colleagues' evidence-based checklist intervention, encompassing hand hygiene, maximal sterile barrier precautions, chlorhexidine skin antisepsis, avoidance of the femoral site, and prompt removal of unnecessary catheters, produced a large and sustained reduction, up to 66%, in CRBSI rates across more than 100 participating intensive care units, a magnitude of benefit achieved through process and insertion-bundle measures alone, without any catheter-surface technology [17]. This finding is essential context for interpreting the heparin-coating literature: catheter coating, whether heparin-based or antiseptic-based, should be understood as an adjunct to, not a substitute for, rigorous insertion and maintenance bundle compliance, and national guideline bodies have consistently framed impregnated and coated catheters as a secondary consideration reserved for settings where baseline bundle-compliant CRBSI rates remain unacceptably high [5,4].

Within that adjunctive role, several limitations temper enthusiasm for heparin coating specifically as the preferred coating technology in sepsis. The head-to-head comparative trial evidence, exemplified by Carrasco and colleagues' finding that chlorhexidine-silver sulfadiazine catheters achieved lower colonization rates than heparin-coated catheters in a general intensive care population, and the CATCH trial's pediatric demonstration that impregnated catheters (using non-heparin antimicrobial technology) reduced bloodstream infection in a large randomized cohort of children requiring central access for reasons including sepsis, together indicate that more recently developed antiseptic and antimicrobial coatings have, in several direct or indirect comparisons, matched or exceeded heparin coating's colonization- and infection-prevention performance [8,18]. Heparin coating also carries a theoretical safety consideration largely absent from antiseptic coatings, namely the risk of heparin-induced immune sensitization or, in rare cases, heparin-induced thrombocytopenia from a continuously heparin-exposed intravascular surface, a consideration that has not been systematically quantified across the trials reviewed here but that warrants explicit surveillance in any sepsis population selected for heparin-coated catheter placement given the baseline thrombocytopenia risk already conferred by sepsis-associated coagulopathy [12].

At the same time, several considerations argue for continued, targeted evaluation of heparin coating in sepsis specifically rather than its wholesale replacement by antiseptic technologies. The Abdelkefi trial's substantial relative risk reduction against uncoated controls, the Pierce trial and the Shah and Shah Cochrane review's dual thrombosis-and-infection benefit with a clinically meaningful number needed to treat, and the mechanistic rationale linking sepsis-associated coagulopathy directly to the thrombosis-infection axis that heparin coating targets, together suggest that heparin-coated catheters may hold a particular comparative advantage precisely in the coagulopathic, thrombosis-prone septic patient, a subgroup not specifically isolated in the general intensive care or pediatric trials reviewed above [7,11,12]. The emergence of next-generation heparin-network coating chemistries engineered to deliver simultaneous, durable antithrombotic and antibacterial activity represents a promising avenue for resolving the historical trade-off between heparin's thrombosis-prevention strength and its comparatively inconsistent colonization-prevention performance relative to antiseptic catheters, and future randomized trials of such multifunctional coatings, specifically enrolling septic or septic shock patients and reporting CRBSI, catheter thrombosis, and heparin-related adverse events as co-primary outcomes, represent the most direct path toward establishing heparin-based catheter technology's precise role in modern sepsis care [6].

Conclusion

The published literature on heparin-coated and heparin-bonded catheters describes a technology with a mechanistically coherent, dual rationale, reduction of the fibrin substrate and thrombogenic surface that both promotes catheter thrombosis and shelters biofilm-forming organisms, and clinical trial evidence that is real but heterogeneous in magnitude and comparative standing [3,4]. Against uncoated catheters, heparin coating has produced a substantial and statistically significant CRBSI reduction in a dedicated adult hematology-oncology trial and a clinically meaningful number needed to treat in the pooled pediatric Cochrane evidence, alongside a demonstrated reduction in hemodialysis catheter bacteremia [7,12,15]. Against newer antiseptic-impregnated catheters, however, heparin coating has more often shown a comparative disadvantage in general critically ill populations, and the large pediatric CATCH trial's positive result for non-heparin impregnated catheters reinforces that heparin coating is one of several competing coating technologies rather than the clear standard of care [8,9,18]. For sepsis patients specifically, who combine prolonged catheter dwell time, elevated baseline CRBSI risk, and a coagulopathic state that mechanistically links catheter thrombosis to catheter infection, heparin-coated catheters represent a biologically plausible, evidence-supported, but not yet definitively superior adjunct to bundle-based CRBSI prevention, best considered on a case-by-case basis alongside antiseptic alternatives until dedicated, sepsis-specific randomized trials of heparin coating, and of the emerging multifunctional heparin-network coatings now in development, are available to guide selection [17,5,6]. Until such evidence matures, the totality of the literature supports two practical conclusions: first, that rigorous insertion and maintenance bundle compliance remains the dominant, non-negotiable determinant of CRBSI risk regardless of catheter coating; and second, that heparin coating should be regarded as a legitimate, mechanistically distinct option for the coagulopathic, thrombosis-prone septic patient rather than either a default

choice or an obsolete technology superseded entirely by antiseptic catheters.

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Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

Varga P conceived the review, conducted the literature search, and drafted the manuscript. Oja K contributed to literature screening and infectious-disease framing and critically revised the manuscript for important intellectual content. Jansen J contributed additional clinical microbiology context and approved the final version for submission.

Ethics Statement

Not applicable. This is a narrative review of previously published literature and did not involve new experimental data, human participants, or animal subjects.

Data Availability

No new data were generated or analyzed for this review. All sources synthesized are cited in the reference list and are available through their original publishers.

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