Approach to the Infected Catheter

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10.1 Introduction

Vascular access is a continuous challenge for any patient receiving either acute or chronic hemodialysis (HD). The type of access used and its maintenance can impact the outcome of the patient. It is imperative that the practicing nephrologist knows how to deal with complications of vascular access including infections. This chapter will focus on the approach to a patient with an infected catheter.

10.2 Background

Use of central venous catheters (CVC) is essential to the practice of critical care medicine with more than seven million sold annually in the USA [1]. A life-threatening complication of CVC is a bloodstream infection. Approximately 80,000 episodes of catheter-related bloodstream infections (CRBSI) occur in the USA annually at a cost of approximately $25,000–$45,000 per episode [1, 2]. Serious complications of this illness can occur in as many as 44 % of bacteremic episodes making optimal treatment imperative. Serious complications include endocarditis, osteomyelitis, thrombophlebitis, septic arthritis, epidural abscess, and death [3]. These data are not specific to the HD population, but CVC are essential to many patients who require dialysis making management of the infected catheters an important topic for nephrologists.

Over the last decade there has been a push to place fistulas earlier in chronic kidney disease patients. This was started because the United States Renal Data System (USRDS) showed that patients using a catheter were four times more likely to get an infection than those using a graft and eight times more likely than those using a fistula [4]. The Fistula First initiative has decreased the number of chronic kidney disease patients who initiate HD with a catheter, but more than 65 % of US patients will still have their first HD session using a catheter. This is compared to 14 % who use arterial-venous fistulas [5]. With 116,395 incident cases of end-stage renal disease in 2009, this means more than 75,000 patients experienced catheter use at the start of their dialysis careers [5].

Many HD patients are rapidly transitioned to other means of venous access, but the increased risk associated with catheters is imposed on the majority of end-stage renal disease (ESRD) patients at dialysis initiation. The use of CVC as an option for permanent hemodialysis access began in the mid-1980s. Current first-year infection-related mortality is 2.4 times higher than it was in 1981, much of which has been attributed to CVC use [3, 5]. In addition, when comparing total cost of a patient receiving dialysis through an arterial-venous fistula, those with a catheter have a 25 % higher cost, mostly attributed to catheter-related infection costs [5]. The increased mortality from catheter use heightens the already elevated mortality rate for this high-risk population [6]. It is imperative that the dialysis care team works to prevent, suspect, manage, and treat infections related to catheters appropriately as patient outcomes depend on this practice.

10.3 Risk Factors for Infection

Before an infection can be diagnosed, it needs to be suspected. Risk factors have been identified that increase the possibility of an infection. These include recent or prolonged hospitalization, poor patient hygiene, prior catheter-related infection, inadequate dialysis, low albumin levels, diabetes, hypertension, and longer duration of catheter use [1, 3, 7–9]. A review of 96 studies was conducted to highlight common risk factors present for all CVC-related infections. The leading events that increased risk for catheter-related infections include insertion without maximal sterile barriers (relative risk 2.1), placement of a catheter via guidewire exchange

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into an old site (relative risk 2), heavy cutaneous colonization of the insertions site (relative risk 5.5), contamination of the catheter hub, and duration of the catheter for more than 7 days (relative risk 2) [1]. Guidelines to decrease or eliminate these risk factors have been published and are available for review [10].

10.3.1 Mechanisms of Infection

Catheter-related bloodstream infections (CRBSI) can occur by three main mechanisms. Organisms that are present on the skin can gain entry through the exit site of a newly placed catheter. This can occur at the time of initial placement or, in the case of tunneled line placement, before the subcutaneous tunnel has had time to endothelialize. The organism can enter at the catheter exit site and migrate down the path of the catheter on its external surface where it can either colonize the tissue, device, or eventually make it to the bloodstream to be hematogenously spread during hemodialysis [1, 11, 12]. The second mechanism of infection occurs when there is contamination of the catheter hub, usually by contact with patient's skin or clothing or from health-care workers' hands when accessing the catheter. This leads to intraluminal colonization of the catheter and is spread during high blood flows during hemodialysis [12]. Lastly, infections elsewhere in the body can hematogenously seed the catheter as it sits in its venous environment [2].

As quickly as 24 h after insertion, a fibrin sheath can form around the catheter as it occupies its position in the vein [13]. Fibrin can cause difficulty with catheter blood flow but can also promote biofilm formation and be a nidus for infection [14]. The layer of glycomatrix that makes up the fibrin sheath can protect against the effects of antibiotics on the organisms hiding in its layers making clearance with antimicrobial therapy difficult [3]. The biofilm that adheres to the catheter does not universally have colonization of bacteria as was previously believed. This was confirmed by scanning electron microscopy, therefore prevention of colonization may be useful [13].

10.3.2 Suspecting an Infection

Due to an immunocompromised state, patients requiring dialysis may not present with common signs and symptoms of bacteremia, and surveillance cultures are an ineffective way of monitoring for infection [7]. Al-Solaiman et al. investigated the rate of infection and associated symptoms in catheter-dependent HD patients. The study followed 172 catheter-dependent patients over a 1.5-year period of time and found the rate of infection was 4.6 infections per 1,000 catheter days [15]. This was similar to published data that cited rates from 0.6 to 6.5 episodes per 1,000 catheter days [3]. The most common symptoms leading to assessment for infection were fever, rigors, altered mentation, change in exit-site appearance, and unexplained hypotension. Only 47 % of catheter-related bacterial infections presented with fever. In fact, symptoms were evenly distributed between fevers alone, fever and rigors, and rigors alone but as many as 20 % had none of these findings [15]. Therefore, a wide array of symptoms should raise suspicion for catheter-related infection and fever is not a defining criterion (Fig. 10.1).

As the exit site is one of the portals of entry that can lead to catheter-related bacteremia, it is important to do a careful examination whenever there is a change appearance or symptoms are noted. Manipulation of the catheter through daily wear and tear can cause increased erythema, but any drainage, tenderness, or associated fevers should be carefully monitored.

10.3.3 Diagnosis of Suspected Catheter-Related Bloodstream Infection (CRBSI)

Once symptoms suggest that infection is present, blood cultures should be drawn from the catheter and a peripheral site simultaneously. It is important that diligent skin and catheter hub antiseptic practices are followed prior to taking the culture and that the same volume of blood is obtained per culture bottle to have an accurate and comparable measure. If the catheter happens to be immediately removed, the tip should be sent for culture as well [7] (Fig. 10.1).

Two different cultures are done to help differentiate between the infection coming from the catheter and an alternative source. A definitive diagnosis of CRBSI can be made if the same organism is identified from a peripheral culture and the catheter tip. Alternative means of diagnosis includes a quantitative blood culture from the catheter hub that shows a colony count three-fold greater than a culture from the peripheral vein. The same criteria can be used for cultures taken from two different catheter lumens. Lastly, differential time to positivity can assist in diagnosis if the catheter lumen turning positive a minimum of 2 h before the alternative culture [7]. If physical examination reveals drainage at the exit site of the catheter during examination, it should be cultured. The diagnosis of catheter-related infection is strengthened if the same organism is found at both sites [3, 7, 16] (Fig. 10.1).

Given the unique venous access challenges posed by HD patients, attempts to obtain peripheral cultures from veins that may be used for future vascular access should be avoided. The Infectious Disease Society of America (ISDA),

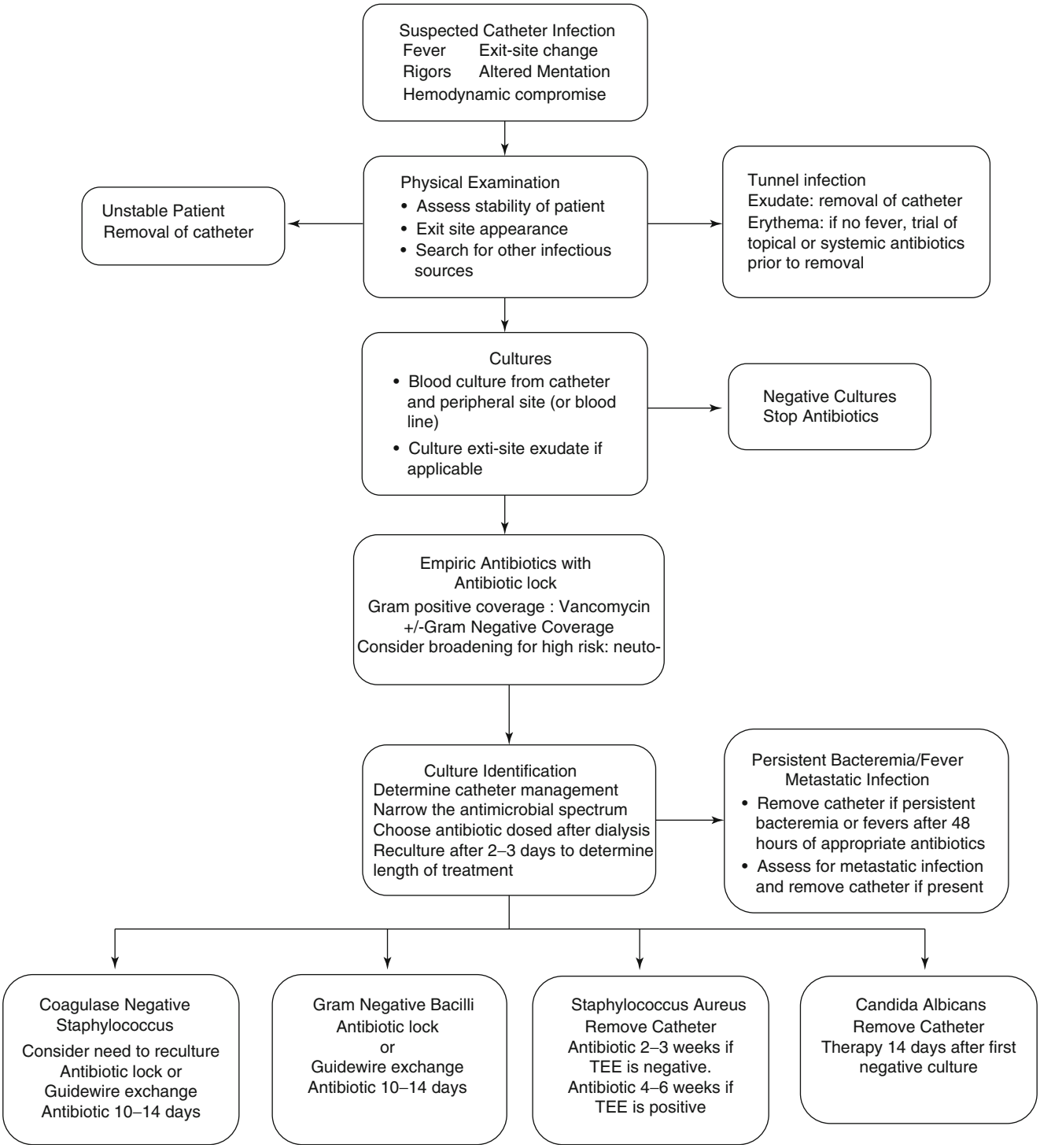

Fig. 10.1 Approach to tunneled catheter-related infection (Information adapted from ISDA Guidelines 2009 and ERA-EDTA of 2010. TEE: Transesophageal echocardiography)

the European Renal Association-European Dialysis and Transplantation Association (ERA-EDTA) have accepted an alternative approach to diagnosis of CRBSI in these patients. If peripheral cultures are not available, cultures can be taken from the CVC and a second set from the bloodline connected to the catheter after HD is started [3, 7, 16]. The high blood flows necessary for HD makes this sample similar to a peripheral assessment.

10.4 Management of Confirmed Infections

10.4.1 Catheter Management

Catheter lock, removal, or guidewire exchange needs to be a part of the treatment plan for CRBSI as there is a high incidence of treatment failure with systemic antibiotics alone [17–19]. Prompt removal of the catheter in any patient with severe sepsis is necessary. In patients who have persistent bacteremia after 48–72 h of appropriate antibiotic therapy, thrombophlebitis, endocarditis, or the presence of any metastatic infection also require catheter removal [17, 20]. Some organisms have been shown to have a high incidence of relapse when these devices are retained. Therefore removal is recommended if *Staphylococcus aureus, Pseudomonas aeruginosa*, fungi, or mycobacteria are identified [7]. The timing of reinsertion of permanent or temporary access for hemodialysis after removal is important to management of infections. Insertion can be considered after the patient has been afebrile for 48–72 h, has normalization of C-reactive protein, and has negative blood cultures [7, 16]. If these parameters are not met and hemodialysis is necessary, a single-use catheter may be placed, but the risk and benefits must be balanced prior to removal [16]. Short-term catheters should be removed if CRBSI is found to be due to gram-negative bacilli, *S. aureus*, enterococci, fungi, and mycobacteria [7].

At times, there are HD patients who have absolutely no alternative sites for vascular access placement. In these situations, it is reasonable to consider either guidewire exchange with an antimicrobial catheter and/or systemic antibiotics with antibiotic lock when any infection occurs [7]. Many studies have been conducted concerning techniques to preserve the current location of the catheter. These evaluated removal of the catheter with delayed replacement, exchanging the catheter over a wire or preservation of the present catheter with use of antibiotic locks in addition to systemic antibiotic administration. The studies are difficult to compare because different end points were used, but it was clearly evident that removal of the catheter was the best way to eradicate the organism. The small success seen with salvage techniques is overshadowed by a failure rate of at least 65 %, and a cost was at least twice as high as other management methods [17].

Current recommendations by the ISDA suggest catheter salvage can be tried using antibiotic lock and systemic antibiotics for uncomplicated infections by organisms other than *S. aureus*, *P. aeruginosa*, Bacillus species, Micrococcus species, propionibacteria, fungi, or mycobacteria. Surveillance cultures should be obtained 1 week after completion of antibiotic course. If blood cultures are persistently positive despite appropriate antibiotics, catheter removal is necessary [7]. Alternatively, if the symptoms prompting suspicion of CRBSI resolve in 2–3 days and none of the aforementioned organisms are present, guidewire exchange can be done without continued antibiotic lock or negative cultures [21– 23]. Risks of this technique include increased sclerosis and stenosis of the venous access; therefore the new catheter may have functional compromise [16].

Exit-site infections leading to bacteremia are more likely to occur in recently placed tunneled line due to skin trauma and decreased time for endothelialization and fibrosis of the catheter tunnel [12]. Both the natural creation of the biofilm, which can harbor organisms, and abscess formation in the tunnel can lead to less antibiotic penetration [24]. Often tunneled line infections are unable to be treated solely with systemic antibiotics and removal of catheters is necessary, especially when fever is present. Topical antibiotics can be attempted for exit-site infections without fevers. If the infection is not quickly cleared, systemic antibiotics should be initiated and catheter removal if this therapy fails [16].

10.4.2 Identifying the Organism

Empiric Therapy

In addition to catheter management, defining the organism that is causing the infection is necessary to determine treatment. Often there are no culture results available at the time when antibiotics are initiated. Guidance to the appropriate antibiotic should be based on local infection trends where available [16]. Fifty to eighty percent of catheter-related infections are due to gram-positive organisms: the most common being *Staphylococcus aureus* or *coagulase-negative staphylococcus* [7, 18]. Given the high incidence of *S. aureus* infections being methicillin resistant, vancomycin or teicoplanin should be the first-line agent for all patients when empiric therapy is started [3, 7, 16]. If the patient is immunocompromised or neutropenic and if the local culture trend in the HD unit has a high incidence of gram-negative organisms, then empiric coverage with third-generation cephalosporin, carbapenem, or b-lactam/b-lactamase combination should be added [11]. Also, if the catheter is in the femoral vein, empiric fungal and gram-negative coverage is recommended [7] (Table 10.1).

Antibiotic locks are included in the 2009 ISDA guidelines as part of empiric therapy when the catheter is retained and cultures are being processed [7]. This therapy should be used in conjunction with systemic antibiotics and not as a monotherapy. A reasonable approach would be to start with a vancomycin antibiotic locks until organism identification is available. Gram-negative organisms respond well to treatment with antibiotic locks as the success rate has been shown to be 87–100 %. This is not true with *S. aureus* with only 40–55 % success rate and is one reason why catheter removal is part of management of infection by this organism [25, 26].

Table 10.1 Recommended duration of antibiotic therapy

Type of infection	Length of antimicrobial treatment
Uncomplicated with line removed	
Coagulase-negative staphylococci	5–7 days
Staphylococcus Aureus	14 days
Enterococcus	7–14 days
Gram-negative bacilli	7–14 days
Candida	14 days
Tunneled infection	
No fungemia or bacteremia, lineremoved	7–10 days
Complicated infection, line removed	
Bacteremia fungemia persists >48 h	4–6 weeks
Endocarditis	
Intravascular infection	6–8 weeks
Osteomyelitis	
Uncomplicated with line retained (not *S. aureus*, *P. aeruginosa*, Bacillus species, Mia-ococcus species, propionibacteria, fungi or mycobacteria)	2 weeks of systemic antibiotics with antibiotic lock
Coagulase-negative staphylococci	or
Gram negative organism	Guidewire exchange with 2 weeks of systemic antibiotics
Enterococcus	

Note that day 1 of therapy is the first day of negative blood cultures after appropriate antibiotics were started

Tailoring Antibiotics

Empiric antibiotics should be adjusted as soon as culture results are available. For example, if *S. aureus* is found to be resistant to vancomycin, a change to daptomycin is indicated [7]. Alternatively, if *S. aureus* is found to be methicillin sensitive, it is worthwhile to change to cefazolin as continuation with vancomycin increases the risk of treatment failure [7, 27]. Blood cultures should be done after 48 h of antibiotic treatment to ensure that the infection is cleared. The day of the first negative culture can be considered day 1 of therapy. Also, tailoring antibiotics to better suit administration with dialysis is preferred. Vancomycin, ceftazidime, or cefazolin can be given after each dialysis session (Fig. 10.1).

Gram-negative species are seen in approximately one-third of the isolates [7, 18]. Most of these organisms are susceptible to aminoglycosides, but the risk of ototoxicity and diminishing any residual renal function makes their use less preferred [7]. Cephalosporins, namely, ceftazidime, are suggested for ease of dosing and low side effect profile. These organisms are rather responsive to treatment and can be managed with systemic antibiotics and antibiotic lock without catheter removal [7]. Guidewire exchange in conjunction with systemic antibiotics is an alternative therapy (Fig. 10.1).

Fungi make up the remaining <10 % of CRBSI. Catheter removal is necessary to treat these infections as prospective studies have shown worse outcomes with catheter salvage management [28–30]. Antibiotic locks are experimental and have not shown good salvage results.

10.4.3 Duration of Antibiotics

When determining the duration of antibiotic therapy, it is important to obtain daily blood cultures after starting antibiotics. The first day when blood cultures are negative is noted to be day 1 of therapy. The treatment timeline varies depending on catheter management strategies and if systemic complications are present. Many infections can be treated with a 7–14-days course, but if severe complications occur, the duration can be extended. For example, if endocarditis is present, treatment will be extended to 4–6 weeks and osteomyelitis will prompt continuation of antibiotics to 8 weeks of therapy [7, 11] (Table 10.2).

10.5 Prevention

The best means to reducing catheter-related infections would be to eliminate catheters. This is not possible in a large number of patients in whom vasculature is not amenable to AV fistula or graft placement. There are a variety of ideas that have been explored as means to reduce the risk of infection.

10.5.1 Sterile Technique in Placement of Catheter

The use of sterile technique including maximal barrier precautions including mask, cap, sterile gown, sterile gloves, and large sterile drape can decrease bloodstream infections

Table 10.2 Antimicrobial therapy for hemodialysis catheter-related bloodstream infections

	Antimicrobial	Dose	Alternative	Notes
Empiric choice				
Gram-positive—use in all suspected cases when cultures pending	Vancomycin	20 mg/kg loading dose then 500 mg during the last 30 min of each HD session	Teicoplanin	No linezolid
Gram-negative—per local susceptibilities/culture pattern usually third or fourth generation cephalosporin	Ceftazidime	1 g IV after each HD	Gentamicin 1 mg/kg after each HD session (max 100 mg)	
If femoral catheter—add gram-negative and yeast coverage	Caspofungin	70 mg IV loading dose then 50 mg IV daily	Micafungin 100 mg IV daily	
If neutropenic—add gram-negative coverage	Ceftazidime	1 g IV after each HD		
Antibiotic lock if catheter retained	Vancomycin	5 mg/mL in heparin or saline	Ceftazidime 0.5 mg/mL	
After culture identified gram-positive				
Staphylococcus aureus				Catheter should be removed
Methicillin sensitive	Cefazolin	20 mg/kg to nearest 500 mg after HD	Vancomycin	Vancomycin shown to have higher failure rate
Methicillin resistant	Vancomycin	20 mg/kg loading dose then 500 mg during the last 30 min of each HD session	Daptomycin 6 mg/kg after dialysis	
Vancomycin resistant	Daptomycin	6 mg/kg after HD	Linezolid 600 mg oral twice daily	
Coagulase-negative staphylococci			If single culture then repeat with peripheral culture; colonization can occur and antibiotic lock may be acceptable	
Methicillin sensitive	Cefazolin	20 mg/kg to nearest 500 mg after HD	Vancomycin or Bactrim	
Methicillin resistant	Vancomycin	20 mg/kg loading dose then 500 mg during the last 30 min of each HD session	Daptomycin 6 mg/kg after dialysis	Linazolid also acceptable
Enterococcus faecalis/faecium				Catheter can be retained
Ampicillin sensitive	Ampicillin	500 mg oral after dialysis		
Ampicillin resistant	Vancomycin	20 mg/kg loading dose then 500 mg during the last 30 min of each HD session	Daptomycin 6 mg/kg after dialysis	
Amp/vancomycin resistant	Daptomycin	6 mg/kg after dialysis	Linezolid 600 mg oral twice daily	
Gram-negative				
Pseudomonas aeruginosa	Cefepime	1 g IV once then 500 mg IV daily after HD	Piperacillin/tazobactam 2.25 mg q 8 h	Catheter should be removed
Escherichia coli and Klebsiella				Catheter can be retained with antibiotic lock or guidewire exchange
ESBL negative	Ceftriaxone	1 g IV daily	Ciprofloxacin 250–500 mg po daily after dialysis or 200 mg IV q 12 h after dialysis	
ESBL positive	Ertapenem	1 g daily	Ciprofloxacin 250–500 mg po daily after dialysis or 200 mg IV q 12 h after dialysis	
Enterobacter	Ertapenem	1 g daily	Cefepime or cipro	Catheter can be retained with antibiotic lock or guidewire exchange
Acinetobacter	Ampicillin/sulbactam	1–2 g IV daily	Imipenem	Catheter can be retained with antibiotic lock or guidewire exchange
Stenotrophomonas	Bactrim		Ticarcillin	Catheter can be retained with antibiotic lock or guidewire exchange
Fungus				Removal of catheter
Candida	Caspofungin	70 mg IV loading dose then 50 mg IV daily	Micafungin 100 mg IV daily	Fluconazole (if C. Krusei or glabrata is low) 200 mg daily

and save approximately $167 per CVC inserted [31, 32]. Also, the use of chlorhexidine can reduce the risk of catheter colonization when compared to other skin-cleaning techniques [33, 34]. No data has shown prophylactic antibiotics at the time of insertion is helpful in preventing catheter-related infections [11].

10.5.2 Vascular Access Team

Often CRBSI occurs in patients in the outpatient dialysis unit who do not need admission to the hospital. Rarely is consideration given to catheter removal as part of their treatment plan as the outpatients are not as ill as those seen in the hospital setting. Implementation of an access-care team for the outpatient hemodialysis setting has been shown to decrease treatment failure and reduce death from sepsis. Much of this success was based on decreased catheter salvage practices [3, 17, 35].

10.5.3 Antibiotic Impregnated Catheters

In the general population requiring CVC, it has been shown that the use of CVC impregnated with chlorhexidine and silver sulfadiazine or minocycline and rifampin has lowered the rate of infection from 7.6 infections per 1,000 catheter days to 1.6 infections per 1,000 catheter days ($P = 0.03$ with CI 0.0–30.95). This was estimated to decrease medical costs by approximately $196 per catheter inserted [36]. This data has not been consistent in the dialysis population; therefore, Kidney Disease Outcomes Quality Initiative (KDOQI) and the IDSA do not have specific recommendations for routine use.

10.5.4 Daily Handling

As per guidelines established from studies on general CVC access placement, all staff accessing catheters should wear masks and gloves as well as perform good hand hygiene regimens [37]. Chlorhexidine and alcohol solutions should be used as antiseptics for exit-site cleanings. This solution has been shown to be superior to povidone-iodine solution when they were directly compared [38].

10.5.5 Exit-Site Care

Studies have shown more than 75 % decreased rate of infection with topical ointment application around exit sites. A Cochrane review was done on topical ointment and found that mupirocin ointment reduced the risk of catheter-related bacteremia, including the infections caused by *S. aureus*, but did not have any effect on infection-related mortality. There was insufficient evidence to show if topical honey or other types of ointments are beneficial [39]. There is no consensus on the optimal frequency of dressing changes or the type of exit-site dressing that is used [3, 33, 39].

10.5.6 Catheter Lock

Many clinical trials have been performed to assess the efficacy of catheter locks containing antibiotics for infection prophylaxis. Of the published trials, it seems that using these locks can reduce the rate of catheter-related infections by as much as 51–99 % [3, 40]. In a systematic review, it was found that the number needed to treat was three patients to prevent 1 CRSBI [41]. The drawback to this practice may be increased antibiotic resistance [3]. Another locking technique has been an attempt to eradicate the biofilm with solutions such as ethylenediaminetetraacetic acid (EDTA) or high-concentration citrate. Successful reduction in biofilm was noted, but data has varied on reducing the time to catheter-related bacteremia [40, 42]. There will be more data on the horizon to establish the optimal use of these solutions to improve patient care.

10.5.7 Scheduled Catheter Exchange

For patients that need prolonged catheterization, no benefit has been seen with routine exchange of the catheter over a wire or schedule replacement of the catheter at a new site. More risk of mechanical complications are present with these protocols [11].

10.6 Summary

Catheters are associated with an increased risk of mortality in the hemodialysis population largely due to their heightened threat of infection. The best means to prevent associated complications is to avoid their use by having arterial-venous fistulas or arterial-venous grafts in place. At times, acute illness or poor vascular access can limit the ability of these alternative forms of vascular access which leaves catheters as the only option for treatment. In these situations, meticulous care for the catheter and prompt recognition and management of infections are important. Continued research on prevention of infections is necessary to decrease the mortality related to catheter use.

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