Infections in Patients with Mechanical Circulatory Support

Emily M. Eichenberger, MD, MHS[a,*], Varun Phadke, MD[b], Lindsay M. Busch, MD[c,d], Stephanie M. Pouch, MD, MS[e]

KEYWORDS

• Mechanical circulatory support • Infection • Ventricular assist device • MCS • VAD • Bacteremia • Fungemia

KEY POINTS

- New ISHLT definitions for MCS infection encompass acute and durable MCS and are broadly categorized into device-specific and device-nonspecific.
- Patients with MCS-specific infections have a higher risk of mortality and lower quality of life than those without infection.
- Optimal treatment of MCS infections hinges on understanding of whether the device is involved and to what extent.
- A multidisciplinary approach to treating MCS infection is critical and includes infectious disease specialists, cardiology and critical care clinicians, and surgeons.
- In general, MCS infection is not a contraindication to heart transplantation.

INTRODUCTION

Mechanical circulatory support (MCS) devices have emerged as life-prolonging interventions in patients with end-stage heart failure, cardiogenic shock, and severe acute respiratory failure. Two major classes of MCS exist: durable and acute. Durable MCS devices, notably left ventricular assist devices (VADs), play a critical role in managing

[a] Department of Medicine, Division of Infectious Diseases, Emory University School of Medicine, 101 Woodruff Circle, WMB, Suite 5125, Atlanta, GA 30322, USA; [b] Department of Medicine, Division of Infectious Diseases, Emory University School of Medicine, 101 Woodruff Circle, WMB, Suite 2101, Atlanta, GA 30322, USA; [c] Department of Medicine, Division of Infectious Diseases, Emory University School of Medicine, WMB, Suite 5127, Atlanta, GA 30322, USA; [d] Emory Critical Care Center, Emory Healthcare, Atlanta, GA 30322, USA; [e] Department of Medicine, Division of Infectious Diseases, Emory University School of Medicine, 101 Woodruff Circle, WMB, Suite 2305, Atlanta, GA 30322, USA
* Corresponding author.
E-mail address: Emily.m.eichenberger@emory.edu
Twitter: @emilymeich (E.M.E.); @VarunPhadke2 (V.P.); @StephaniePouch (S.M.P.)

Infect Dis Clin N Am 38 (2024) 693–712
https://doi.org/10.1016/j.idc.2024.07.005 **id.theclinics.com**

advanced heart failure. They serve as a bridge to transplantation for eligible candidates or as a destination therapy when transplantation is not feasible. Durable VADs may remain in place for many years, requiring removal or device exchange in extreme circumstances. At present, the only commercially available left VAD currently approved for implantation is the Heartmate 3, although some patients harbor older devices, such as the HeartMate 2 and HeartWare HVAD.[1]

Acute MCS comprises temporary devices for cardiogenic shock or severe acute respiratory failure. This category includes a range of devices, such as extracorporeal membrane oxygenation (ECMO), the intraaortic balloon pump, and temporary VADs (including surgical right [CentriMag] and biventricular VADs, percutaneous left [Impella] and right [PROTEKDuo] VADs, and total artificial heart).[1] These devices are percutaneously or surgically implanted for left ventricular, right ventricular, or biventricular circulatory support and are intended for short-term cardiovascular support until organ recovery or transplantation. Venovenous ECMO may be used for respiratory support until organ recovery or transplantation.

Patients on MCS are at heightened risk for infection given the invasive nature of these devices with internal and external components, the surgical implantation of the devices, and the presence of foreign material susceptible to biofilm formation. With rapidly evolving MCS technologies and increasing use in the critically ill population, the need for standardized definitions and approaches to the evaluation and treatment of infection is paramount to improving patient outcomes.

NEW MECHANICAL CIRCULATORY SUPPORT INFECTION DEFINITIONS

In 2011 the International Society for Heart and Lung Transplantation (ISHLT) published a set of standardized definitions for durable VAD infections. With increased use of acute MCS over the past, new definitions were needed to incorporate the infections associated with these devices into the existing framework and improve its clinical applicability. As such, the ISHLT recently updated their guidance, expanding the definitions to encompass durable and acute MCS device infections and to reflect clinically relevant definitions.

Under the new framework, MCS infections are classified into two broad categories: MCS-specific infections or non-MCS-specific infections (**Fig. 1**). MCS-specific infections are infections involving the device itself, and therefore cannot occur in patients without MCS. Non-MCS-specific infections are infections that do not originate from the device hardware, and therefore can occur in patients without MCS. Examples of such infections include infective endocarditis of the native or prosthetic valves, cardiac implantable electronic device infections, sternal wound infections, mediastinitis, and non-MCS bloodstream infections (BSI) arising from a non-MCS source. It is important to note that non-MCS-specific infections can still impact the device, evolving into MCS infections over time, thereby requiring clinicians to remain vigilant for device involvement. This review does not cover non-MCS-specific infections in detail, focusing instead on the nuances and management of MCS-specific infections (**Table 1**).

PERCUTANEOUS LEAD INFECTIONS

Definitions

Percutaneous lead infections are soft tissue infections that can occur anywhere along the tract of the lead that connects the device with an external controller. They are the most common type of MCS-specific infection and can arise at any time postimplantation. Presentation is often characterized by pain, tenderness, erythema, induration, or

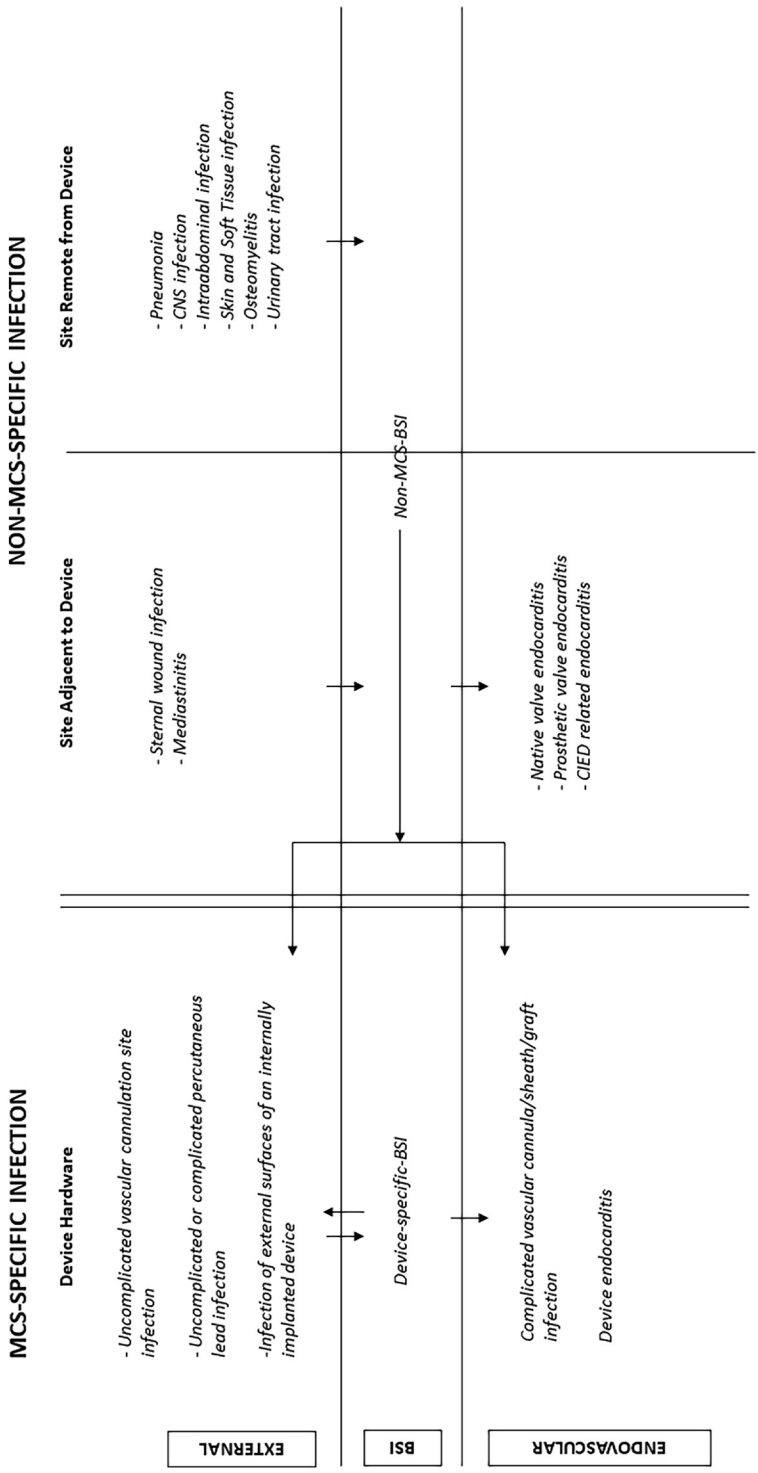

Fig. 1. BSIs in VAD patients. Is the pump involved? CIED, cardiac implantable electronic device; CNS, central nervous system.

Table 1
Overview of mechanical circulatory support infections

	Symptoms	Diagnostics		Management		
Infection Type	Clinical Manifestations	Microbiologic Work-Up	Imaging	Antimicrobials	Surgery	Suppressive Therapy
Uncomplicated percutaneous lead infection	Pain, tenderness, erythema, induration, or purulent drainage at the site of the percutaneous lead/driveline	Drainage culture (bacteria and fungal) Peripheral blood cultures	CT imaging to assess for deeper infection/fluid collection	2-wk IV or highly bioavailable PO antimicrobial therapy	None	No
Complicated percutaneous lead infection	Same as uncomplicated plus 1 or more of the following: • Systemic signs of infection • Fluid collection/ abscess at the exit site • Radiographic signs of lead infection • Growth of multidrug-resistant bacteria or fungus from the exit site • Positive blood cultures • Signs of infection on the external surface of the implanted device			IV therapy for 4–8 wk	Surgical drainage of abscess with or without repositioning and wound vacuum-assisted closure application	Yes

Uncomplicated vascular cannula site infection	Pain, erythema, tenderness, and/or drainage at cannulation site	Drainage culture (bacterial and fungal) Blood cultures (peripheral and from MCS circuit, when applicable)	None	2–4 wk of IV or highly bioavailable PO antimicrobial therapy	None	No
Complicated vascular cannula/ sheath/graft infection	Same as uncomplicated plus 1 or more of the following: • Systemic symptoms of infection • Growth of a multidrug-resistant organism or fungus • Positive blood cultures • Presence of a fistulous tract or fluid collection at the insertion site • Purulence at the interface between the cannula or sheath and blood vessel, or at graft-anastomosis site	Drainage culture (bacterial and fungal) Blood cultures (peripheral and from MCS circuit, when applicable) Tissue/vascular graft cultures (bacterial and fungal)	Direct surgical visualization	4–8 wk of IV antimicrobial therapy	Surgical washout/ debridement and drainage of any abscess Device exchange may be considered in extreme scenarios	Yes: until device explant
Infection of the external surfaces	Systemic signs/ symptoms of	Blood cultures (peripheral and from MCS circuit,	CT or ultrasound of the affected area Consider PET/CT	4–8 wk of IV antimicrobials	Surgery to drain fluid collection and debride	Yes: until device explant

(*continued on next page*)

Table 1
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	Symptoms	Diagnostics			Management	
of an implantable component	infection may be present Pain or erythematous skin over the infected implanted component may be present	when applicable) CT-guided aspiration of fluid collection or surgically collected tissue specimen from infected area	when CT unrevealing and concern for infection remains		infected tissue Device exchange may be considered in extreme scenarios	
Device-specific bloodstream infection	Positive peripheral blood culture along with 1 or more of the following: • Infection involving percutaneous lead, cannula, sheath, graft, or external surface of the implantable device • Positive culture of any component of the device after explant • Persistently positive blood culture with same organism >72 h Systemic signs and symptoms of infection may also be present	Blood cultures (peripheral and from MCS circuit, when applicable) Tissue, fluid, or vascular graft cultures if obtained in setting of surgical debridement	TEE > TTE	≥6-wk IV antimicrobials	Surgical drainage of any abscesses or fluid collections	Yes: until device explant

Device-endocarditis	Positive peripheral blood and/or MCS circuit blood culture with 1 or more of the following: • Thrombus or vegetation on intravascular aspect of device component (pump/cannula) • Cerebrovascular accident consistent with septic emboli Systemic signs and symptoms of infection may also be present	Blood cultures (peripheral and from MCS circuit, when applicable) Tissue, fluid or vascular graft cultures if obtained in setting of surgical debridement	TEE > TTE Cardiac CT Consider 18-FDG PET/CT or leukocyte scintigraphy when TEE and CT unrevealing	≥ 6-wk IV antimicrobials	Surgical drainage of any abscesses or fluid collections Device exchange may be considered in extreme scenarios	Yes: until device explant

Abbreviations: IV, intravenous; TTE, transthoracic echocardiogram.

purulent drainage at the site of the percutaneous lead/driveline, although signs of infection can be more subtle, presenting only with serous drainage or wound dehiscence.[2] The ISHLT further categorizes percutaneous lead infection into complicated and uncomplicated. Complicated percutaneous lead infection is diagnosed by any one of the following signs: systemic signs of infection (ie, fever, leukocytosis, systemic inflammatory response syndrome, or sepsis), fluid collection or abscess at the exit site, radiographic signs of lead infection, growth of multidrug-resistant (MDR) bacteria or fungus from the exit site, concurrent positive blood cultures, or signs of infection on the external surface of the implanted device. In the absence of all these complicating factors, the infection is considered an uncomplicated percutaneous lead infection.[1]

Epidemiology

Percutaneous lead infections are frequently the result of mechanical trauma, such as accidental tugging on the external driveline.[3] Reports of host risk factors for percutaneous lead infections are inconsistent across the literature, although obesity is frequently cited, likely because of immune dysregulation, impaired healing, and hygiene challenges associated with increased abdominal adiposity.[4,5] Other risk factors include exposed driveline velour[6,7] and prolonged duration of device implantation.[8]

The most common microbial etiologies include gram-positive skin flora including *Staphylococcus aureus*, coagulase-negative *Staphylococci*, *Streptococcus pyogenes*, and *Streptococcus agalactiae*, and *Pseudomonas aeruginosa*.[2,9–13] Enterobacterales and *Enterococcus* species have also been implicated in percutaneous lead infections,[12] and to a lesser extent, *Candida* species.[2,11]

Diagnosis and Management

A detailed history, lead exit site cultures, blood cultures, and targeted imaging with ultrasound or computed tomography (CT) to detect abscesses or fluid collections are essential to differentiate between complicated and uncomplicated infections. Uncomplicated infections may be managed with 2 weeks of intravenous or oral antibiotics targeted to the causative pathogen without surgery.[2] Suppressive antibiotic therapy is not typical after the first episode of an uncomplicated percutaneous lead infection. However, because of the propensity for biofilm formation along the velour or other artificial components of the device, it is likely that colonization will persist and infection reoccur.[14,15] With recurrent episodes, suppressive antibiotics may be warranted. Strategies to reduce risk of recurrence include ensuring driveline immobilization and counseling on driveline hygiene.[2]

Complicated percutaneous lead infections necessitate longer treatment durations with parenteral or highly bioavailable oral antimicrobials for 4 to 8 weeks. Surgical intervention may be required for abscess drainage or driveline repositioning.[2] The use of a wound vacuum-assisted closure system at the debridement site can aid in healing, reduce bacteria colonization, and prevent fistula formation.[16–18] Posttreatment, long-term suppressive antimicrobial therapy is often recommended because of the high risk of relapse or progression.[2]

VASCULAR CANNULA SITE AND COMPLICATED VASCULAR CANNULA/SHEATH/GRAFT INFECTIONS

Definitions

Vascular cannulation site infections manifest with localized symptoms, such as pain, erythema, tenderness, and/or drainage, and can occur either at the time of cannulation or subsequently because of inoculation by surrounding flora. These are limited to the site of the cannula insertion and do not extend endovascularly and do not

involve the graft/sheath. Systemic signs of infection are absent, and imaging does not demonstrate any evidence of a fluid collection or abscess.

Complicated vascular cannula/sheath/graft infection involves deeper infection beyond the cannula insertion site, infection of the endovascular space surrounding the cannula, and/or infection between the cannula sheath/blood vessel or graft-anastomosis site. Presence of any of the following indicate a complicated vascular cannula/sheath/graft infection: systemic symptoms of infection (eg, fever, systemic inflammatory response syndrome, sepsis, or leukocytosis); growth of an MDR organism; positive blood cultures; presence of a fistulous tract or fluid collection at the insertion site; and purulence at the interface between the cannula or sheath and blood vessel, or at the graft-anastomosis site.[1]

Epidemiology

The risk of vascular cannula infection varies across MCS devices, with reported incidences of approximately 2.4% for Impella cannulae,[19] 3% for venovenous-ECMO cannulae,[20] and 10% for venoarterial ECMO sites.[21] Percutaneous RVAD (ie, PROTEKDuo) cannulation site infections seem to be less frequent, although specific incidence rates are not well-documented.[22–24] Device duration is proportionate to infection risk.[25]

Common pathogens for any cannula infection include gram-positive skin flora, such as *S aureus* and coagulase-negative *Staphylococci*, and *P aeruginosa*. Additionally, cannula location often influences the cause of infection. For example, femoral ECMO cannulation infections may exhibit a higher incidence of enteric gram-negative bacteria cannula infections.[20,21,26–29] Candida species, although less common, are also capable of causing vascular cannula infections.[20]

Diagnosis and Management

Diagnostic evaluation of suspected vascular cannula infection involves a detailed history, wound culture from the cannulation site when feasible, blood cultures, and ultrasound or CT imaging to evaluate for fluid collection. There is a paucity of published data on the management of uncomplicated vascular cannulation site infections. Typically treatment involves 2 to 4 weeks of antibiotic therapy, depending on organism isolated and ability to remove or exchange affected catheters. Suppressive therapy is generally not indicated. The treatment of complicated vascular cannula/sheath/graft infections necessitates a longer duration ranging anywhere from 4 to 8 weeks because of endovascular involvement. Surgical intervention for abscess drainage is recommended. Antibiotic suppression is typically continued until all MCS hardware has been completely removed to prevent the recurrence or spread of infection.

Management of retained infected endovascular grafts in patients who have undergone MCS explant and heart transplant requires careful consideration. Surgical removal of the infected graft is generally advised to eliminate the source of infection.[30] For those with retained infected grafts posttransplant, the continuation of suppressive antibiotics is prudent; however, the optimal duration of antibiotic therapy is unclear[4,31] and is subject to clinical discretion based on the patient's clinical response and overall trajectory.

INFECTION OF THE EXTERNAL SURFACES OF AN IMPLANTABLE COMPONENT

Definition and Presentation

Infection of the external surfaces of an implantable component is an infected fluid collection or infected tissue surrounding the external (extravascular) surface of a

pump, cannula, or any other component implanted within the body. Because these are extravascular infections, blood cultures may not be positive. Patients may present with fever, leukocytosis, systemic inflammatory response syndrome, or sepsis.[1] In some cases, patients may present with pain over the implanted component, erythema of the skin overlying the device, or even a fistulous tract formation.

Epidemiology

Infection of the external surfaces of an implantable component of the MCS device may arise as an extension of a complicated percutaneous lead infection, inoculation at the time of implantation, or contiguous infection that develops from an adjacent site of infection (eg, mediastinitis).[2] Coagulase-negative *Staphylococcus*, *S aureus*, *Enterococci*, and *P aeruginosa* are among the most common microbial causes of infection.[2,32,33]

Diagnosis

Peripheral and MCS circuit blood cultures should be collected.[1] Ultrasound or CT of the affected area should be performed but have limited sensitivity in detecting VAD infections. Nuclear imaging, specifically 18F-fluorodeoxyglucose PET imaging with CT (18-FDG PET/CT) may be helpful, and is further discussed in the Device Endocarditis: Diagnostics section.[34] CT-guided aspiration or surgical specimen collection of fluid is recommended to tailor antimicrobials.[1,2]

Management

As with other types of MCS-related infections, infection of the external surfaces of an implantable component is virtually impossible to eradicate without complete device explant. Reduction in the burden of infection with surgery is often necessary, along with a 4- to 8-week course of intravenous antibiotic therapy, with the exact duration depending on source control and whether there is coincident BSI. Suppressive antibiotics are usually prescribed until complete device explanation.[2]

BLOODSTREAM INFECTION

Definitions and Clinical Presentation

BSI pose a significant challenge in patients with MCS. These infections are classified into two categories: device-specific BSI and non-MCS-specific BSI. Device-specific BSI involve the device components, such as the percutaneous lead, cannula, sheath, graft, or external surface of the implanted device. Non-MCS BSI originate from sources unrelated to the MCS device. Importantly, non-MCS-specific BSIs may evolve into MCS-specific infections if the device becomes secondarily seeded by the BSI. This review largely focuses on MCS-specific BSI.

Epidemiology of Mechanical Circulatory Support–Specific Bloodstream Infections

A review of MCS, including left VAD, total artificial heart, right VAD, and biventricular assist device, enrolled in the International Registry for Mechanically Assisted Circulatory Support between 2013 and 2015 revealed that 12% of patients with MCS developed a BSI in the first 3 months after implant. Nearly 86% of these episodes were non-MCS in origin, of which 91% were bacterial and 6% fungal. Device-specific BSIs were most frequently secondary to driveline infections: 97% bacterial and 2% fungal.[35]

The incidence of BSI in acute MCS ranges from 8% to 15%, with 7% to 43% being MCS-specific. The microbial cause of BSI in acute MCS patients mirrors that of durable MCS, with common pathogens including coagulase-negative *Staphylococcus*, Enterobacterales, *Enterococcus* species, and *P aeruginosa*.[20,31,36–40] Fungal BSI is

less common, but when present is often caused by *Candida* species. Candidemia in patients with MCS is more likely to indicate a device-related BSI than non-device-related BSI, and is associated with high mortality.[18,29,38,39,41–43] Indications of device-specific BSI include persistent bacteremia, isolation of MDR organisms, or candidemia.[41,44]

In patients with MCS, a range of host factors contribute to the risk of BSI: elevated body mass index,[35,45] poor nutritional status,[41] older age,[46] frailty before MCS implantation,[35] diabetes or hyperglycemia,[47] and history of reoperation.[41] The use of total parenteral nutrition is an independent risk factor for candidemia in patients with MCS.[42]

Clinical Presentation

Device-specific BSI may manifest with fever, leukocytosis, low cardiac output, or signs of systemic inflammatory response syndrome or sepsis.[48] BSI in patients on ECMO is more subtle because fevers are often masked by the cooling of blood as it traverses the extracorporeal circuit.[38] Additionally, leukocytosis may either be absent or misleading in ECMO patients. Activated white blood cells can adhere to the oxygenator, resulting in artificially lower white counts and conversely, leukocytosis is often nonspecific in the setting of critical illness. Systemic inflammation and white blood cell demargination in response to the mechanical circuit may occur, particularly early after ECMO initiation.[49–52] Therefore, close monitoring of hemodynamics and careful, daily evaluation of cannula sites should be performed. Any suspicion for BSI in patients on ECMO or other MCS should prompt collection of two sets of blood cultures.

Diagnosis

Determination of MCS device involvement in the setting of BSI is challenging. Blood cultures should be drawn from the periphery and the MCS circuit, if applicable. Surveillance blood cultures should be obtained until negative. Persistently positive blood cultures (eg, >72 hours) are indicative of a device-specific BSI.[31] Clinicians should document a careful history and perform thorough examination for retained sources of infection. If the source of infection includes one of the device components or if there is no identifiable source of infection, the patient should be considered to have an MCS-specific BSI for management purposes. Presence of *S aureus*, *P aeruginosa*, or *Candida* spp in blood cultures should raise suspicion for device-specific BSI and should be managed as such. Echocardiography should be performed if a patient has one of these three pathogens or persistently positive blood cultures because of any pathogen to evaluate for endocarditis.

Management

Prompt initiation of appropriate, bactericidal intravenous antimicrobials is essential. In the setting of sepsis, empiric coverage for methicillin-resistant *S aureus* and *Pseudomonas* spp should be started.[2] Clinicians should review the patients' prior microbiology reports in conjunction with infectious disease consultation whenever possible to ensure that empiric therapy adequately covers those pathogens, particularly given that MDR organisms are common in this population. In unstable patients with significant risk factors for candidemia (ie, use of total parenteral nutrition, history of MCS-specific *Candida* infection, or use of ECMO), clinicians should consider adding an empiric antifungal agent, although minimal data exist to support this practice.

Once a pathogen is isolated, antibiotics should be tailored accordingly. Duration of treatment is at least 6 weeks and should be followed with suppressive antimicrobials until device explanation. Suppressive therapy may need to be intravenous if no oral option is available. Surgical debridement of any identified fluid collections or

abscesses should be performed when present[2] because the likelihood of failure of medical therapy alone is exceedingly high in this setting.

Special consideration should be given to antibiotic dosing and frequency in patients on ECMO. Antibiotic pharmacokinetics and pharmacodynamics are significantly altered in ECMO because of circuit sequestration, altered glomerular filtration rate from continuous flow, and specific antimicrobial properties. Antibiotic dosing for ECMO is beyond the scope of this manuscript, but can be reviewed in detail elsewhere.[53,54]

DEVICE ENDOCARDITIS

Definition and Clinical Presentation

One of the most serious complications of BSI in a patient on MCS is device endocarditis. Device endocarditis is an infection of the intravascular aspect of the device, such as the cannulas or pump. The diagnosis is based on echocardiographic or radiographic evidence of a vegetation or thrombus on the intravascular aspect of the cardiac device or evidence of septic emboli (eg, cerebrovascular emboli) in the setting of a positive peripheral or MCS circuit blood culture. Similar to patients with device-specific BSI, patients with device endocarditis may present with fever, leukocytosis, low cardiac output, systemic inflammatory response syndrome, or signs of sepsis.[48] Patients may also show evidence of embolic phenomena on examination.

Epidemiology

Device endocarditis is responsible for approximately 15% to 22% of infections in VAD patients,[42,55] with the most common causative pathogens being *S aureus*, coagulase-negative *Staphylococci*, *Enterococci*, *P aeruginosa*, and *Candida* spp.[48,55–58] Risk factors include diabetes mellitus; older age; and undergoing implantation, extraction, or replacement of an implantable cardioverter defibrillator post VAD installation.[55,58] Device endocarditis in the setting of acute MCS remains underexplored and warrants further research.

Diagnosis

Peripheral blood cultures and blood cultures obtained from the MCS circuit are recommended as part of the diagnostic evaluation of device endocarditis.[1] Initial diagnostics should include echocardiography, with transesophageal echocardiography (TEE) preferred over transthoracic echocardiogram, and cardiac CT. These imaging techniques can detect fluid collections suggestive of abscess, or a lead vegetation. However, the sensitivity of echocardiography and cardiac CT is limited, because of difficulty of the echocardiogram to visualize the endovascular surface of the device, and streak artifact caused by the device in CT.[48,56,59]

In cases where echocardiography and CT are unrevealing yet suspicion for device involvement remains high, nuclear imaging, specifically 18-FDG PET/CT, may be helpful.[34] PET/CT has emerged as a useful tool in infective endocarditis and cardiac device infections[60] and is now included in the European endocarditis valve endocarditis guidelines[61] and modified Duke criteria for diagnosis of endocarditis.[62] PET/CT imaging has shown high accuracy in diagnosing VAD-related infections, with reports of sensitivity ranging from 92% to 95% and specificity ranging from 83% to 91%.[63,64] PET/CT has the advantage of potentially diagnosing infections earlier than cardiac CT and TEE and may identify extracardiac foci of infection, such as septic emboli.[59,65] However, PET/CT may be less specific in the early postimplantation setting given increased uptake of FDG at the site of recent surgery, and it may have limited capabilities in detecting biofilms.[34,66,67]

Leukocyte scintigraphy, also known as a tagged white blood cell scan, has also been proposed as an alternative strategy to detecting MCS device infection when CT and echocardiography are inconclusive. Although highly sensitive for detection of cardiac implantable electronic device infections, leukocyte scintigraphy seems to have lower sensitivity relative to PET/CT in diagnosing durable VAD infections.[68,69] Limitations of nuclear imaging include cost, exposure to ionizing radiation, and challenges of timely access in an inpatient setting, making echocardiography and CT practical first-line imaging options when evaluating MCS device infection. PET/CT and leukocyte scintigraphy may serve as valuable second- and third-line diagnostic strategies, respectively, when TEE and CT are inconclusive yet the suspicion for MCS-specific infection remains. CT or MRI of the brain may be indicated if septic emboli to the central nervous system are suspected.[1]

Management

Management of device endocarditis requires a multidisciplinary approach. As with device-specific BSI, immediate initiation of intravenous antimicrobials is critical, and includes empiric coverage of methicillin-resistant *S aureus*, *Pseudomonas*, and any prior MDR organisms. Patients who develop sepsis on MCS that are receiving TPN, or patients on ECMO support may benefit from an empiric antifungal, although this has not been fully evaluated in the literature. Treatment duration is at least 6 weeks, followed by suppressive therapy until device explant. Intravenous suppressive therapy may be required if no oral option exists. Surgical debridement of any identified fluid collections or abscesses should be performed, and device exchange may be required in extenuating cases, as discussed further in the Device Exchange Considerations section.[2]

CONSEQUENCES OF MECHANICAL CIRCULATORY SUPPORT INFECTIONS

Patients with MCS-specific infections have a higher risk of mortality and lower quality of life than those without infection.[70,71] An INTERMACs study found that the 24-month survival for durable VAD patients with infection was 59% relative to 74.8% for those who never developed infection.[70] Infection is also the leading cause of readmission among patients with durable VAD.[72] Patients with MCS-specific infections are at risk for recurrent/persistent infections because of the inability to completely eradicate biofilm from the hardware. Consequently, patients often require prolonged courses of intravenous antibiotics followed by suppressive therapy. This extended antibiotic use increases the risk of catheter-associated complications, such as peripherally inserted central catheter thrombosis and catheter-related BSI, antibiotic-induced kidney injury, *Clostridium difficile* colitis, the development of antimicrobial resistance, and lower overall quality of life.[73,74] Lastly, among patients awaiting heart transplantation, those with MCS-specific device infections experience longer waiting times compared with their uninfected counterparts.[55,75]

DEVICE EXCHANGE CONSIDERATIONS

MCS device exchange for difficult-to-control MCS-specific infections is typically a last resort intervention. The benefits of device exchange as compared with medical therapy alone have not been thoroughly evaluated, and device exchange carries a significant risk of mortality.[56,76,77] In the rare instances where a device is exchanged, great care should be taken at the time of surgery to thoroughly wash out the anatomic space and antibiotic therapy should be continued after exchange given the high likelihood of infection relapse.[76,77]

HEART TRANSPLANTATION IN PATIENTS WITH MECHANICAL CIRCULATORY SUPPORT–SPECIFIC INFECTIONS

In the setting of organ nonrecovery, heart transplantation remains the only curative modality for MCS device infection. In general, MCS device infection should not prevent patients from undergoing heart transplantation except in cases of septic shock or active mold infection.[2] Patients with MCS-specific infections do not exhibit a higher risk of posttransplant mortality compared with uninfected patients, provided that they are not in septic shock at the time of transplantation.[31,75] In patients with MCS-specific BSI without septic shock, heart transplantation may be safe 48 to 72 hours from first negative blood cultures.[31]

The optimal duration of antibiotics after heart transplant is unknown. Longer antibiotic courses (eg, 4–6 weeks) may be given to patients with positive intraoperative cultures or extensive native tissue infection, whereas 14 days may be adequate if intraoperative cultures are negative and there was no recent preoperative BSI.[78]

AREAS FOR FUTURE RESEARCH

Role of Bacteriophages in Treatment

The frequency of MDR infections in VAD patients coupled with the poor penetration of antibiotics into biofilms and limitations of surgical debridement significantly limit the ability to successfully treat MCS infections. Bacteriophages, which are viruses that infect bacteria, are an appealing addition to the current therapeutic repertoire.

Successful use of bacteriophage therapy has been reported in some, but not all, patients with durable VAD infections.[79–82] Advantages of bacteriophages include their ability to circumvent antibiotic resistance, their antibiofilm properties, and the ability to coadminister with antibiotics. Use of bacteriophages as adjunctive treatment of MCS device infection requires further study; in particular, the indication, the route, optimal dose strategy, and duration of the phage therapy.

Fecal Microbiota Transplant

MDR bacteria and *Candida* infections present a major challenge in MCS patients, with nearly one-third of infections classified as MDR.[83] MCS patients are at increased risk of MDR organism colonization and infection given their nosocomial exposure and prolonged, and often indefinite durations of antimicrobial therapy. An area of emerging research is the application of fecal microbiota transplant to reduce intestinal colonization and infection with MDR organisms. A recent randomized controlled trial in kidney transplant recipients demonstrated fecal microbiota transplant to be an effective strategy in MDR organism decolonization and prevention of MDR infection.[84] Patients with durable MCS who have complicated percutaneous lead infections, device endocarditis, or infection of the external surfaces of an implantable component are ideal candidates in which to study the efficacy and durability of fecal microbiota transplant in reducing MDR bacteria colonization.

SUMMARY

The use of acute and durable MCS is increasing. The updated ISHLT MCS infection definitions effectively bridge the gap between durable and acute MCS infections, providing unifying definitions that are clinically relevant. The ability to appropriately treat MCS patients with infections hinges on an understanding of whether the device is involved and to what extent. Recognition of the different components and nuances of each device shapes the diagnostic evaluation of these infections. A multidisciplinary approach that includes infectious disease specialists, cardiology and critical care clinicians, and surgeons is essential for optimal management.

CLINICS CARE POINTS

- Uncomplicated percutaneous lead infections may be managed with 2 weeks of intravenous or oral antibiotics targeted to the causative pathogen without surgery, and suppressive antibiotic therapy is not typical after the first episode of an uncomplicated percutaneous lead infection.
- Patients with a complicated percutaneous lead infection often require long-term suppressive antimicrobial therapy.
- Vascular cannula site infection is typically treated with 2 to 4 weeks of antibiotic therapy, depending on organism isolated and ability to remove or exchange affected catheters, and is not typically followed by suppressive therapy.
- Complicated vascular cannula/sheath/graft infections require 4 to 8 weeks of antimicrobial therapy along with surgical intervention for abscess drainage. Antibiotic suppression is typically continued until all MCS hardware has been completely removed.
- Patients with infection of the external surfaces of an implantable component may not exhibit positive blood cultures.
- PET/CT may be of use in evaluating presence and extent of MCS device infection.
- Indications that the patient may have a device-specific BSI include persistent bacteremia $\geq$72 hours, isolation of multidrug-resistant organisms, or candidemia.
- Candidemia in a patient with MCS is more likely to indicate a device-related BSI than non-device-related BSI and is associated with an exceedingly high risk of mortality.

DISCLOSURE

The authors have nothing to disclose.

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