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Trends in the Management of Infective Endocarditis for Patients Who Inject Drugs: A Survey of Healthcare Facilities in Tennessee

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Background. The current endocarditis management strategies among Tennessee healthcare facilities for people who inject drugs (PWID) were evaluated.

Methods. This was a survey-based study of healthcare facilities that treat infective endocarditis in PWID within Tennessee. The primary outcome of the study was to describe current practice among facilities regarding the treatment of endocarditis in PWID, including approaches to addiction management, antimicrobial therapy, and cardiac surgery.

Results. There were 17 facilities that responded to the survey but only 16 facilities completed the entire survey. Although 15 facilities (88%) responded that they evaluate patients for substance use disorders on admission, only 4 (24%) of those facilities offered addiction consultation service. Regarding antibiotic therapy, most facilities offered completion of intravenous antibiotic course inpatient or at a skilled nursing facility (94% and 75%, respectively). Other treatment options less commonly offered by facilities included: transition to oral antibiotics (56%), use of long-acting lipoglycopeptides (50%), and outpatient parenteral antibiotic therapy (25%). Of the 16 facilities that completed the survey, only 7 performed cardiac surgery and 6 performed catheter-based interventions.

Conclusions. Although most facilities surveyed offered completion of antibiotic therapy either as inpatient or at a skill nursing facility, they were less likely to offer alternative options such as home infusion antibiotics, long-acting antibiotics, or oral antibiotic treatment for endocarditis. Most facilities screened for substance abuse on admission, but few provided addiction services. There may be an opportunity to enhance care for PWID through alternative antibiotic therapies and addiction services.

Keywords. endocarditis; intravenous drug use; persons who inject drugs; PWID; *Staphylococcus aureus*.

Infective endocarditis is a serious and potentially life-threatening infectious disease [1]. Over the past more than 20 years, there has been an increase in the number of hospitalizations related to endocarditis [2]. Although the number of hospitalizations has increased, there has been an overall decrease in the number of endocarditis-related mortalities with a notable exception: young adults aged 25 to 44 years with a concomitant substance use disorder saw a significant increase in mortality [3]. There appears to be a correlation between states at the epicenter of the opioid crisis and an increase in endocarditis mortality rates, with Tennessee being 1 of those 3 states [2]. Studies have also found that people who inject drugs (PWID) have a longer length of stay in the hospital during treatment compared to those who do not [4]. It is well-known that injection drug use is considered a predisposition to the development of both infective endocarditis and methicillin-resistant *Staphylococcus aureus* (MRSA) infections [5]. Parikh et al found that approximately 25% of MRSA bloodstream infections in Tennessee between 2015–2017 were attributed to PWID [6]. In that same time period, >40% of bloodstream infections in PWID involved endocarditis, compared to only about 10% in patients who did not inject drugs.

Current standards of care, logistical complications, and organizational challenges may also play a role in the complexity of treating endocarditis in this patient population. Hospitals may face challenges with unplanned discharges, limited resources and staffing to address underlying addiction management, provider stigmatization, and a lack of clearly defined policies. The objective of this survey was to determine the current endocarditis management strategies being utilized in the State of Tennessee for PWID.

METHODS

This was a survey-based study engaging healthcare facilities that care for PWID diagnosed with infective endocarditis.

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The primary outcome of the study was to describe facilities' current practice regarding the treatment of endocarditis in PWID in the State of Tennessee, focusing on 3 domains: mental health services, antimicrobial therapy, and surgical intervention. This survey did not involve human subject research and therefore did not require the approval or exemption of an institutional review board.

The survey involved a questionnaire that consisted of 4 main sections: (1) demographic information, (2) addiction management, (3) antimicrobial therapy, and (4) cardiac surgery (Supplementary Appendix 1). Responses to most questions were captured as a binary ("yes" or "no") or as a 4-point unipolar rating scale (1 = rarely, 2 = sometimes, 3 = usually, 4 = always). The questionnaire was designed with branch logic (or skip logic) so that facilities might be asked additional questions depending on their response to the previous question. The survey was sent via email to facility representatives that participate in a bimonthly Antibiotic Steward Call through the Tennessee Department of Health. Participation in the survey was voluntary, and the questionnaire was estimated to take about 10 minutes.

The survey was conducted electronically between November 2022 and January 2023. Facilities were included if they were in Tennessee, indicated they treated patients with endocarditis, and completed at least part of the survey. Only 1 respondent from each facility was permitted. Study data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Vanderbilt University [7]. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for data integration and interoperability with external sources.

Partially completed surveys were included in analysis if they completed at least 33% of the survey. One of the respondents to the survey did not treat patients with infective endocarditis at the facility and was therefore excluded from the study. Another respondent did not complete any sections of the questionnaire. One investigator independently reviewed the responses, with a second investigator reviewing the data for discrepancies and verification.

RESULTS

Of the 17 facilities included in the survey, 16 (94%) completed all sections. More than half of the respondents to the survey were community hospitals (59%). The majority of the facilities (59%) that responded identified as facilities with greater than 300 beds (Table 1). The survey respondents represented facilities from 10 different counties in Tennessee and consisted of 16 pharmacists (94%) and 1 infectious diseases physician (6%).

Table 1. Demographics of Facilities Surveyed (n = 17)

Characteristic	N (%) of Responses
Facility type	
– Community hospital	10 (59%)
– Academic medical center	6 (35%)
– Long-term acute care	1 (6%)
– Critical access hospital	0
– Veterans Affairs hospital	0
Facility bed size	
– >300	10 (59%)
– 100–300	4 (23%)
– <100	3 (18%)

Addiction Management

The majority of facilities surveyed (88%) indicated that they evaluated patients at the facility for substance use disorders on admission, either "sometimes' (41%) or "always' (47%). Two respondents were "unsure" of their facility's procedure for evaluating patients for substance abuse disorders. However, only 4 (24%) of the facilities surveyed offered addiction consultation service or had addiction-trained clinicians to assist with care. There were 11 facilities (65%) that offered inpatient medications to address opioid withdrawal, such as buprenorphine, methadone, and naltrexone. Of those 11 facilities, only 6 (55%) indicated they made efforts to ensure continuation of addiction care upon hospital discharge.

Antimicrobial Therapy

Facilities were surveyed about the treatment options offered to PWID when treating infective endocarditis. The majority of the facilities (94%) allowed or required patients to complete the full treatment course of IV antibiotics inpatient at the hospital (Table 2). Most facilities (75%) also offer PWID the option to complete the intravenous antibiotic course at a skilled-nursing facility (SNF). Facilities were much less likely to allow PWID to discharge with a central line to complete IV antibiotics as outpatient parenteral antibiotic therapy (OPAT) compared to other treatment options. Of the 4 facilities that allowed patients to complete antibiotics with OPAT, 3 (75%) required a contract or agreement with patients regarding a commitment to either abstinence or substance use disorder treatment to qualify. Half of the facilities offered PWID the ability to complete therapy using long-acting lipoglycopeptides (i.e., dalbavancin or oritavancin) at outpatient infusion centers. More than half of the facilities (56%) indicated they would allow PWID to transition to an oral antibiotic before or upon hospital discharge to complete the full antibiotic course.

When asked about treatment options for PWID when patients leave or threaten to leave against medical advice

Table 2. Treatment Options Offered by Facilities (n = 16)

Treatment Options	N (%)	Rarely	Sometimes	Usually	Always
Complete IV antibiotic course inpatient in the hospital	15 (94%)	1	8	5	1
Complete IV antibiotic course at an SNF	12 (75%)	0	4	8	0
Discharge patient to complete IV antibiotic course as OPAT	4 (25%)	2	2	0	0
Offer long-acting lipoglycopeptides[a] at infusion centers	8 (50%)	4	3	1	0
Transition to oral antibiotic course prior to or upon hospital discharge	9 (56%)	2	5	1	1

Abbreviations: OPAT, outpatient parenteral antibiotic therapy; SNF, skilled-nursing facility.

[a]Such as dalbavancin or oritavancin.

Table 3. Treatment Options Offered by Facilities for Patients Who Leave Against Medical Advice (n = 16)

Treatment Options	N (%)	Rarely	Sometimes	Usually	Always
Complete IV antibiotic course at an SNF	8 (50%)	1	4	2	1
Discharge patient to complete IV antibiotic course as OPAT	1 (6%)	1	0	0	0
Offer long-acting lipoglycopeptides[a] at infusion centers	6 (38%)	3	3	0	0
Transition to oral antibiotic course before or upon hospital discharge	14 (88%)	6	4	4	0

Abbreviations: IV, intravenous; OPAT, outpatient parenteral antibiotic therapy; SNF, skilled-nursing facility.

[a]Such as dalbavancin or oritavancin.

Table 4. Comparison of Treatment Options Offered by Academic Medical Centers and Community Hospitals

Treatment Options N (%)	Academic Medical Centers (n = 6)	Community Hospitals (n = 9)
Complete IV antibiotic course inpatient in the hospital	5 (83%)	9 (100%)
Complete IV antibiotic course at an SNF	5 (83%)	7 (78%)
Discharge patient to complete IV antibiotic course as OPAT	3 (50%)	1 (11%)
Offer long-acting lipoglycopeptides[a] at infusion centers	5 (83%)	3 (33%)
Transition to oral antibiotic course before or upon hospital discharge	5 (67%)	5 (56%)

Abbreviations: IV, intravenous; OPAT, outpatient parenteral antibiotic therapy; SNF, skilled-nursing facility.

[a]Such as dalbavancin or oritavancin.

(AMA), most of these offerings decreased (Table 3). Half of the facilities that completed the survey would allow patients to leave the hospital without continuation of antimicrobial treatment for bacterial endocarditis. Only 1 facility (6%) stated they would discharge PWID with a central line to complete IV antibiotic course as OPAT when leaving AMA. The number of facilities that offered long-acting lipoglycopeptides at infusion centers upon discharge also decreased when comparing planned discharges to AMA (50% vs 38%). However, the number of facilities that would allow transitioning PWID to an oral antibiotic course before or upon hospital discharge increased when comparing planned discharges to AMA (56% vs 88%).

When comparing responses from academic medical centers and community hospitals (Table 4), facilities that would discharge PWID to SNF to complete intravenous antibiotic treatment were similar (83% vs 78%, respectively). Academic medical centers indicated they were less likely to complete the entire intravenous antibiotic course inpatient compared to community hospitals (83% vs 100%). However, academic medical centers were more likely than community hospitals to discharge PWID to complete course as OPAT (50% vs 11%), offer long-acting lipoglycopeptides at outpatient infusion centers (83% vs 33%), and transition to oral antibiotics as step-down therapy (67% vs 56%).

Current endocarditis treatment guidelines recommend treatment for at least 2 to 6 weeks for *S aureus* endocarditis [1]. Facilities were queried about offering treatment courses shorter than 6 weeks for *S aureus* endocarditis in PWID. Only 4 facilities (25%) indicated they would offer a shorter course of antibiotic treatment. Three of those facilities were community hospitals, compared to just 1 academic medical center that would offer shorter treatment courses.

Surgical Intervention

Seven of the 16 facilities (44%) performed cardiac surgery for patients with endocarditis. Of those 7 facilities, 6 (86%) indicated they "sometimes' perform valve replacement surgery for patients with native valve endocarditis in PWID, whereas only 1 (14%) selected "rarely." When those facilities were asked if they perform valve replacement surgery for PWID who had

previously undergone valve replacement, only 3 (43%) answered "sometimes," compared to 4 (57%) who chose "rarely." Of the 16 facilities that completed the survey, only 6 (38%) indicated that they perform catheter-based interventions, such as AngioVac (AngioDynamics, Latham, NY), for PWID with tricuspid valve endocarditis.

DISCUSSION

The severity and prevalence of infective endocarditis in PWID cannot be understated. PWID have a 16-fold increase in developing invasive MRSA infections compared to those who do not inject drugs [8]. Approximately 85% of right-sided endocarditis cases in PWID are attributed to *S aureus* [9]. A recent systematic review and meta-analysis found that *S aureus* bacteremia was associated with a 30-day and 1-year mortality rate of 18% and 30%, respectively [10]. Equally concerning is the number of patients who complete the full course of antibiotic therapy for invasive *S aureus* infections. A recent observational cohort study found a significantly lower antibiotic completion among PWID compared to those who did not inject drugs (70% vs 87%), which led to double the risk of recurrent or persistent infection within 1 year [11]. In that same study, researchers found that about 25% of PWID with *S aureus* infections involved a patient-directed discharge, such as leaving the hospital AMA.

This is the first study, to our knowledge, to describe current strategies utilized by healthcare facilities in the State of Tennessee for the treatment of endocarditis in PWID. This survey questionnaire was based heavily on the recent scientific statement regarding the treatment of endocarditis in PWID published by Baddour et al [9]. That publication highlighted alternative treatment strategies other than simply retaining patients in the hospital to complete the full course of antibiotic therapy.

Traditionally, treatment for endocarditis has consisted of continuing the intravenous antibiotics through completion, either in the inpatient hospital setting or in a setting that can provide acute care or skilled nursing outside of the hospital. Stigma surrounding addiction and mental health may serve as a barrier to providing adequate care outside of the hospital setting. In recent years, several potential outpatient treatment options for endocarditis have been studied and may be increasingly attractive options for both patients and healthcare facilities.

Many patients without a history of injectable drug use are routinely offered the option of discharging from the hospital with central venous access, such as a peripheral inserted central catheter, to complete OPAT. Because of concern that central venous access outside of the healthcare facility setting in PWID would lead to use of that central line to inject illicit drugs, many providers have not traditionally allowed this treatment option for this patient population. Our survey results reflect that hesitancy, with only one quarter of respondents indicating they offer OPAT to this patient population on hospital discharge. However, there is growing evidence that OPAT can be successfully and safely achieved in PWID despite these concerns. Suzuki et al reviewed 10 studies that evaluated OPAT in PWID and found that there was no difference in completion of therapy, mortality, or adverse events related to catheters when compared to patients who do not use injectable drugs [12]. They did note that hospital readmission rates may be higher in PWID, but the readmission rates varied greatly between studies. The most effective strategy with OPAT may involve the combination of OPAT and concurrent addiction treatment. A retrospective study by Price et al examined the feasibility and safety of this approach [13]. Patients had to meet certain eligibility criteria to qualify for OPAT and buprenorphine therapy, including safe housing, abstinence from illicit substance use, and agreeing to return for follow-up appointments. Of the 20 patients that met criteria for OPAT, there were no deaths or overdoses reported. Although 3 patients did relapse and inject drugs during OPAT, none of the 3 patients used the peripheral inserted central catheter line when they relapsed. There was no significant difference in 30-day readmission between patients discharged with OPAT and patients who were not. A small, pilot randomized trial at the University of Kentucky Medical Center compared patients with substance use disorders who were randomized to either OPAT (n = 10) or completion of intravenous antibiotics inpatient (n = 10) [14]. All patients received assessment and treatment for substance use disorders by an addiction management physician, consultation of an infectious disease provider, had follow-up appointments with an outpatient physician at least weekly, and received buprenorphine therapy both in-hospital and after discharge. Not surprisingly, the hospital length of stay was much lower in the OPAT group compared to usual care (22.4 days vs 45.9 days, respectively). There is currently a larger study ongoing to expand that pilot study to more patients [15]. Although the results of these studies of OPAT in combination with buprenorphine are promising, both studies were small and strongly susceptible to selection bias regarding the patients. Literature has also shown OPAT in a medical respite or residential treatment facility could save tens of thousands of dollars per episode of OPAT, compared to hospital costs [16, 17].

Long-acting lipoglycopeptides are another potential option for discharging PWID. There are 2 commercially available long-acting lipoglycopeptides, dalbavancin and oritavancin, but neither is currently Food and Drug Administration–approved for the treatment of endocarditis. Although there is a growing body of literature regarding the use of these medications for severe infections, the evidence is still limited. A systematic review of long-acting lipoglycopeptides in complicated infections identified only 9 studies with 128 total patients that were treated for endocarditis with either dalbavancin or

oritavancin [18]. The median success rate of therapy (defined as resolution of signs and symptoms of infection and either blood culture sterilization, normalized laboratory values, or no further need for antibiotics) was 68% (interquartile range 56–86) for endocarditis. This systematic review also found that for complicated infections, the adverse event rate was about 13% for long-acting lipoglycopeptides, with the most common adverse event being gastrointestinal. Dalbavancin is the most commonly used long-acting lipoglycopeptides for endocarditis and bloodstream infections in the literature, but these studies are mostly retrospective cohort or observation studies that included a small number of patients with endocarditis [19–22]. Most of these studies showed high clinical cure rates in the general study population (44%–100%), shorter hospital stay, similar mortality to standard of care, and low incidence of adverse effects. It is important to note that most patients in these studies received other antibiotic therapy and some achieved sterilization of blood cultures before switching to dalbavancin. The recently completed but unpublished study, Dalbavancin as an Option for Treatment of Staphylococcus Aureus Bacteremia (DOTS Trial), will provide valuable insight (NCT04775953) [23, 24]. Preliminary results presented at the European Society of Clinical Microbiology and Infectious Diseases global meeting in 2024 showed no difference in clinical efficacy and safety between 2 doses of dalbavancin compared to standard-of-care antibiotic therapy [25].

Another approach to treating endocarditis in PWID to avoid prolonged hospitalization is using oral antibiotics. This approach has become an option with increasing attention since the 2019 publication of the Partial Oral Treatment of Endocarditis (POET) trial [26]. Although the POET trial was a large, well-designed, randomized, multicenter trial that compared intravenous only versus transition to oral antibiotic therapy, there were several limitations to fully correlating the results to PWID. First, only patients with left-sided endocarditis were included, but the majority of PWID develop right-sided endocarditis. Indeed, only 2 patients (1%) in the oral therapy group had a history of intravenous drug use. Second, only 23% of patients treated with oral antibiotics in the POET trial had *S aureus* (no patients had MRSA). Perhaps the more insightful study for PWID was the more recent multicenter, retrospective, cohort study published by Freling et al [27]. This was a real-world study that included 257 patients between 2018 and 2022 treated for infective endocarditis with either intravenous or oral stepdown antibiotic therapy. Of the 46 patients treated with oral antibiotics, 37% had a history of intravenous drug use and 35% had right-sided endocarditis of the tricuspid valve. Unlike the POET trial, this study also had much higher rates of *S aureus* endocarditis, accounting for 63% of the patients receiving oral therapy, with 35% of those patients having MRSA. There was no significant difference in 90-day clinical success, mortality, recurrence of infection, or hospital readmission between the 2 groups. There were significantly fewer adverse drug events reported in the oral group compared to the IV group (8.7% vs 27.5%), primarily acute kidney injury (2.2% vs 10.9%) and line-related events (0% vs 8.1%). Another retrospective cohort analysis compared outcomes in PWID with complicated *S aureus* bacteremia [28]. Patients either received the full intravenous antibiotic course inpatient, partial intravenous antibiotics followed by discharge with oral antibiotics, or partial intravenous antibiotics followed by discharge without oral antibiotics (incomplete therapy). The primary endpoint of this study was a composite endpoint of microbiologic treatment failure, which included 90-day readmission due to infection, clinical worsening, new isolation of *S aureus* from a sterile site, or death from infection. Of the 238 patients included in the study, 154 patients (65%) had infective endocarditis. The primary outcome occurred much more in the patients who received incomplete therapy compared to patients who received either complete intravenous therapy or partial oral therapy (44.4% vs 10.7% vs 13%). There was no significant difference in the primary outcome between those who received complete IV therapy or partial oral therapy (10.7% vs 13%). Most patients who received partial oral antibiotics received antibiotic adherence support (including free antibiotics for uninsured patients) and substance use disorder care.

The current American College of Cardiology/American Heart Association guidelines recommend including addiction specialists as part of the treatment team [29]. PWID are at an increased risk of recurrent infective endocarditis, readmission, and mortality compared to individuals who do not inject drugs [30]. To reduce this risk, the underlying issue of addiction must be effectively addressed. Studies have shown that a combination of behavioral interventions along with pharmacotherapy, such as opioid substitution therapy, is needed to decrease relapse rates estimated to be between 60% and 81% at 1 year or less without pharmacotherapy [31]. By lowering relapse rates and effectively treating opioid use disorder, overall outcomes for PWID may be improved.

Cardiac valve replacement surgery is not always indicated for infective endocarditis. Indications for surgery include persistent infection despite antibiotic therapy, advanced heart failure, abscess, and embolic risk [32]. Although surgical risk is low with initial valve surgery in PWID because of younger age and fewer comorbidities, they have a higher risk of relapse and recurrent infection [33]. In fact, PWID have higher mortality risk within 1 year after surgery compared to patients who do not inject drugs. Catheter-based interventions may be a useful alternative to open-heart surgery in patients with right-sided endocarditis for debulking vegetations, especially those who are at high risk for surgery [8]. While debulking may reduce the risk of pulmonary embolism and remove vegetations, it is important to note that this does not treat valve dysfunction or remove all infected material.

One of the major limitations to our study is the small sample size due to low response rate to the survey. According to the Tennessee Hospital Association, there are >180 hospitals throughout 95 counties in Tennessee [34]. This survey captured only a small percentage of those hospitals throughout just 10 counties. Potential next steps include expanding this study to more hospitals in Tennessee and even to a nationwide survey of the treatment of bacterial endocarditis in PWID. Another limitation of this study is that it only focused on policies, procedures, and practices of healthcare facilities. It did not delve into the thoughts, feelings, or perceptions of providers regarding the treatment of endocarditis in PWID. Those types of questions could give valuable insight into the barriers to implementing alternative treatment strategies for these patients. Although this survey asked specific questions regarding mental health and substance abuse evaluation procedures, the participants were not in the field of mental health counseling or addiction management. Likewise, there was no representation from cardiothoracic surgery in the study population. The results of these queries should therefore be interpreted with caution. This study was not designed to investigate the clinical outcomes (such as hospital length of stay, mortality, and/or treatment failure). Future studies evaluating the effectiveness of these interventions on clinical outcomes are needed.

CONCLUSIONS

The majority of facilities surveyed in Tennessee offered completion of antibiotic therapy either as inpatient or at a skill nursing facility. Other treatment modalities such as home infusion antibiotics, long-acting antibiotics, or oral antibiotics were offered by facilities less often. Despite a high number of facilities that indicated they screen for substance abuse on admission, few facilities offered addiction counseling or services. Based on the results of this survey, there may be an opportunity to enhance care for PWID through alternative antibiotic therapies and addiction support services.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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