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Tricuspid valve endocarditis in people who inject drugs: strategies to reduce mortality and recurrent infection

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Tricuspid valve infective endocarditis (TV-IE) in people who inject drugs (PWID) has become an increasingly important clinical and public health concern, driven largely by the expanding opioid epidemic. Although PWID with TV-IE are typically young and often lack major comorbidities, they experience disproportionately high rates of mortality, reinfection, and recurrent hospitalizations. Repeated intravenous injection introduces contaminated particulate matter and pathogens into the venous circulation, promoting microbial adherence to the tricuspid valve, with *Staphylococcus aureus* including methicillin-resistant strains remaining the predominant pathogen. Clinical presentation commonly includes fever, chills, and pulmonary symptoms caused by septic emboli, while diagnostic evaluation relies on multiple blood cultures and echocardiographic assessment, complemented by computed tomography when pulmonary complications are suspected. Approximately 90% of right-sided TV-IE cases can be managed medically, highlighting the importance of optimized antimicrobial therapy tailored to the organism, disease severity, and patient-specific factors. Outpatient parenteral antibiotic therapy (OPAT) remains controversial in PWID, warranting individualized strategies to ensure treatment continuity, particularly in patients at risk of leaving the hospital before completing therapy. Surgical intervention follows standard right-sided IE criteria, with tricuspid valve repair preferred when feasible. Tricuspid valvectomy or emerging percutaneous debulking approaches may serve as adjunctive or temporizing strategies. Addiction treatment is central to improving outcomes, as ongoing injection drug use remains the strongest driver of reinfection and preventable mortality. Early involvement of addiction medicine and initiation of medication-assisted treatment can significantly improve long-term engagement. Optimal management requires a multidisciplinary approach that integrates cardiology, cardiac surgery, infectious disease, and early initiated as well as continued addiction treatment follow-up, behavioral health support, and social services to reduce reinfection risk and support recovery. This review summarizes current evidence regarding epidemiology, microbiology, clinical presentation, and management, with a focus on reducing mortality and preventing recurrent infection in PWID with TV-IE.

Keywords: Tricuspid valve disease; infective endocarditis (IE); people who inject drugs (PWID); intravenous drug use (IVDU); management

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Introduction

Tricuspid valve infective endocarditis (TV-IE) is a challenging clinical scenario, and its incidence is closely related to intravenous drug use (IVDU) (1-3). TV-IE in PWID presents a unique clinical paradox: affected individuals are typically young and without substantial chronic comorbidities apart from IVDU, yet they face disproportionately high rates of morbidity, reinfection, and long-term mortality (4). The prevalence and characteristics of people who inject drugs (PWID) vary substantially across regions, and this epidemiologic heterogeneity translates directly into regional differences in the proportion of TV-IE attributable to IVDU. It is broadly estimated that TV-IE associated with IVDU accounts for approximately one-third of all TV-IE cases in the United States (5). Short-term management and long-term prognosis are closely linked to the underlying substance use disorder. Optimal outcomes therefore depend on a comprehensive, multidisciplinary care model in which the Endocarditis Team is expanded to incorporate addiction-medicine expertise, ensuring that clinical management targets both the infection and the substance use disorder. This review summarizes current evidence on the epidemiology, microbiology, clinical presentation, diagnostic strategies, and therapeutic management of TV-IE in PWID, highlighting approaches to reducing mortality and preventing recurrent infection.

Clinical presentation and diagnostic work-up

PWID is a predisposing condition defined as a minor criterion in the 2023 European Society of Cardiology modified diagnostic criteria for IE (1). IVDU-associated TV-IE typically represents a younger patient population, often without major comorbidities other than substance use disorder, yet with higher rates of HIV and viral hepatitis compared with other patients with right-sided IE (6). Repeated intravenous injections introduce contaminated particulate matter and pathogens directly into the venous circulation, promoting bacterial adherence to the tricuspid valve and right-heart chambers (7). Left-sided IE in PWID is common, with half of all patients displaying left-sided involvement and approximately one-third presenting with isolated left-sided IE (8).

Clinically, patients usually present with fever and chills, accompanied by pulmonary manifestations such as pleuritic chest pain, cough, dyspnea, or hemoptysis caused by septic pulmonary emboli (9). Cardiac murmurs may be subtle or absent due to the low-pressure right-sided circulation,

while right-sided heart failure can occur as a consequence of severe tricuspid regurgitation or pulmonary hypertension resulting from repeated septic embolization. As pulmonary symptoms often predominate and closely mimic primary pulmonary pathology, TV-IE is frequently misattributed to lung-related disease, resulting in delays in accurate diagnosis and timely management.

Essential aspects of the physical examination in PWID include inspection of the skin (to evaluate previous and current injection sites for inflammation or induration), assessment for cirrhosis, evaluation of oral health, and monitoring for signs of substance withdrawal (2). When an additional focus of infection is identified, timely percutaneous or surgical source-control interventions may be required, as persistent infectious foci can lead to relapsing IE. *Staphylococcus aureus*, including an increasing prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA), is the predominant pathogen. Polymicrobial and *Candida* infections are not uncommon in the setting of nonsterile injection practices, particularly in immunocompromised PWID (10,11). Similar to other cases of suspected IE, diagnosis typically relies on multiple blood culture sets and echocardiography (1,2). Transthoracic echocardiography (TTE) is frequently diagnostic given the anterior position of the tricuspid valve and the generally large vegetations seen in right-sided IE. Transesophageal echocardiography (TOE) should be performed in cases with poor TTE image quality or without unequivocal echocardiographic findings. Furthermore, TOE is useful to exclude left-sided IE or pulmonary valve involvement, assess the degree of valvular dysfunction, and exclude abscess formation, intracardiac shunts, or intracardiac fistulae caused by the infectious process. With an increasing incidence of left-sided IE in PWID, the threshold to perform TOE should be low.

Finally, computed tomography is particularly valuable for delineating pulmonary complications of TV-IE, including septic emboli, pulmonary infarcts, and abscess formation. Accordingly, when clinical suspicion is high, computed tomography is the imaging modality of choice.

Antibiotic therapy

Approximately 90% of right-sided TV-IE cases, including those in PWID, can be managed successfully with medical therapy alone, making optimized antimicrobial management the central component of care (12). Empirical antimicrobial therapy in PWID with TV-IE must cover *Staphylococcus aureus*, with regimen selection informed by local MRSA

prevalence, suspected pathogens related to drug type and solvent, and the initial clinical presentation. First-line empirical treatment typically consists of a penicillinase-resistant penicillin, vancomycin, or daptomycin, with the addition of gentamicin considered according to current European guideline recommendations (1). In specific contexts such as pentazocine injection, coverage for *Pseudomonas* species may be necessary (13,14). A history of “brown heroin” dissolved in lemon juice and the presence of large vegetations should raise suspicion for non-*albicans* *Candida* infection, prompting early antifungal therapy, particularly in immunocompromised PWID (15). Once causative organisms are identified, therapy should be tailored appropriately. A randomized controlled trial indicates that a 2-week course of oxacillin or cloxacillin without gentamicin may be sufficient for uncomplicated methicillin-sensitive *Staphylococcus aureus*, provided the patient exhibits good clinical and microbiologic response, vegetation size is ≤ 20 mm, and there is no metastatic infection, empyema, extracardiac complication, prosthetic material, or left-sided involvement (16). Standard 4–6-week regimens remain appropriate when these conditions are not met or when alternative antimicrobial classes are required (17). In selected cases where intravenous therapy is impractical, oral ciprofloxacin combined with rifampin may be considered for TV-IE caused by *Staphylococcus aureus*, provided the strain is susceptible to both drugs, the case is uncomplicated, and patient adherence is monitored carefully (18). Outpatient parenteral antibiotic therapy (OPAT) remains a controversial aspect of care in PWID with TV-IE. Although observational studies suggest that selected PWID can successfully complete OPAT in ambulatory settings, current ESC guidelines do not recommend routine OPAT in this population. Due to the high rate of patient-directed discharges among individuals with IVDU-associated TV-IE occurring before a full treatment plan is established, an individualized strategy incorporating partial-oral regimens or OPAT may help maintain treatment continuity while balancing safety, adherence, and patient preference (19). In this setting, long-acting lipoglycopeptides such as dalbavancin, administered intravenously with once-weekly or biweekly dosing, may facilitate treatment completion in patients for whom prolonged conventional therapy is difficult to implement (20,21).

Surgical management

The consensus is that it is reasonable to avoid surgery when

possible in IVDU-associated TV-IE (2). Although cohort studies demonstrate that cardiac surgery is associated with improved short-term mortality, its impact on long-term prognosis remains debatable (8). Registry data indicate increased long-term mortality in PWID undergoing surgery (hazard ratio 1.80; 95% confidence interval: 0.95–3.30) with the most common cause of death being relapse or a recurrent episode of IE (approximately 55%) (7). Prognosis is strongly correlated with the rate of continued IVDU, which is as high as 70%, even after surgery for IE and in countries with well-established social medical services such as Norway (22).

In general, surgery is recommended for patients with (I) right ventricular dysfunction secondary to acute severe tricuspid regurgitation that is non-responsive to diuretics; (II) persistent vegetation with respiratory insufficiency requiring ventilatory support after recurrent septic pulmonary embolism; (III) large residual vegetation (>20 mm) after recurrent septic pulmonary emboli; (IV) persistent bacteremia/sepsis after ≥ 7 days of appropriate antibiotic therapy; and (V) simultaneous involvement of left-heart structures (1). The indications for surgical intervention in IVDU-associated TV-IE are therefore aligned with those for non-IVDU cases. In clinical routine, however, surgical interventions may be limited to cases of failing conservative therapy based on a multidisciplinary evaluation within the Endocarditis Team, including addiction-trained clinicians. Of note, due to the high rate of metastatic or additional infections in PWID for whom surgery is considered, achieving complete infection control is essential to minimize postoperative complications and reduce the risk of reinfection (3).

When feasible, tricuspid valve repair is preferable to replacement, as it is associated with lower reinfection risk and avoids prosthetic material in patients at high risk for recurrent bacteremia (11,23). However, the extensive tissue destruction frequently observed in PWID often precludes repair (24,25). Prosthesis choice in those requiring replacement is also complex. Although mechanical valves may be considered in younger patients, their use in PWID is complicated by concerns around poor adherence to anticoagulation and inconsistent access to follow-up care (26). Bioprosthetic valves are therefore frequently selected in clinical practice, despite the younger age profile of PWID. Large observational data indicate that IVDU is an independent predictor of worse long-term survival, increased recurrence, and reoperation, yet among PWID, there appears to be no significant difference in susceptibility

to recurrent infection or long-term outcomes between mechanical and bioprosthetic valves (27). Pacemaker management warrants particular consideration in patients undergoing tricuspid valve replacement. Current European IE guidelines recommend placement of a prophylactic epicardial pacing lead at the time of surgery (1), which can be tunneled transthoracically and stored in a subcutaneous pocket, thereby preserving future pacing options while avoiding transvalvular leads that could damage the prosthesis or increase reinfection risk.

In selected individuals, tricuspid valvectomy without prosthetic replacement may be considered, particularly when concerns regarding ongoing IVUD render prosthetic reinfection likely. Valvectomy can serve as an initial stabilizing strategy, allowing time to identify patients who subsequently self-select as candidates for staged valve replacement after achieving abstinence.

In a subset of high-risk patients with large vegetations, recurrent septic pulmonary emboli, or hemodynamic instability who are poor candidates for immediate surgery, percutaneous debulking of intra-atrial septic masses has emerged as an adjunctive therapeutic option aimed at reducing infectious burden and promoting clinical stabilization (28,29). While evidence remains limited, percutaneous debulking may represent a valuable option for selected patients.

Addiction treatment

As clearly stated in the American Heart Association/American College of Cardiology (AHA/ACC) scientific statement on the management of IE in PWID, treating IE alone without concomitant addiction treatment for substance use disorder is failing to treat the underlying cause of illness, an ideal that is a principal tenet in all other medical conditions (2). Patients hospitalized with serious IVUD-associated infections including TV-IE should be evaluated by an Endocarditis Team including addiction medicine specialists as early as possible (1). Consultation teams provide patient-centered support, assist with withdrawal and craving management, and help guide complex clinical decisions during what are often lengthy hospital stays. While PWID may use substances other than opioids, opioid withdrawal is most effectively managed by medications for opioid use disorder (MOUD) including buprenorphine or methadone. These treatments provide rapid symptom relief and help reduce the risk of

patient-directed discharge, ultimately improving early outcomes (30). However, access to addiction-trained providers remains limited in many healthcare settings, despite their clear benefit.

Similarly, regarding long-term outcomes, effective addiction treatment is essential for PWID with prior TV-IE, as continued substance use is the primary driver of reinfection, recurrent hospitalizations, and excess mortality (31). Hospitalization for TV-IE represents a pivotal window during which patients may be especially receptive to treatment engagement, and existing evidence supports initiating MOUD during the inpatient admission (32). These effects are not reproduced by psychosocial interventions alone (33). Counseling-only strategies perform significantly worse than MOUD, and no added benefit has been observed from cognitive behavioral therapy, contingency management, or similar adjunctive interventions when layered on top of MOUD (34). Current evidence therefore supports offering all PWID prompt, low-barrier access to MOUD, with psychosocial services provided as an optional adjunct rather than a requirement.

Follow-up and long-term outcomes

A comprehensive, multidisciplinary management strategy is required to mitigate the risk of recurrent infection, support ongoing recovery, and optimize long-term health (Figure 1). For PWID with previous TV-IE, long-term outcomes are mainly influenced by consistent access to addiction treatment and the capacity to maintain abstinence or substantially reduce harmful use.

Mortality at the index hospitalization for patients with IVUD-associated IE is lower compared with non-IVUD IE (7). This is most likely due to a higher incidence of right-sided IE, younger age, and fewer concomitant comorbidities such as renal failure, pre-existing cardiac disease, or heart failure (4). However, lower short-term mortality does not translate into favorable long-term outcomes due to a return to or continuation of IVUD and recurrent or relapsing IE. As early as 3 months, the readmission rates after index hospitalization have been reported to be between 22% and 49%, with about one-third of patients relapsing into IVUD again at time of readmission (35). Regarding long-term follow-up, overall survival is <50% at 10 years in PWID with left- and/or right-sided IE (7).

After discharge, ongoing follow-up with cardiology and infectious disease specialists, in combination with behavioral

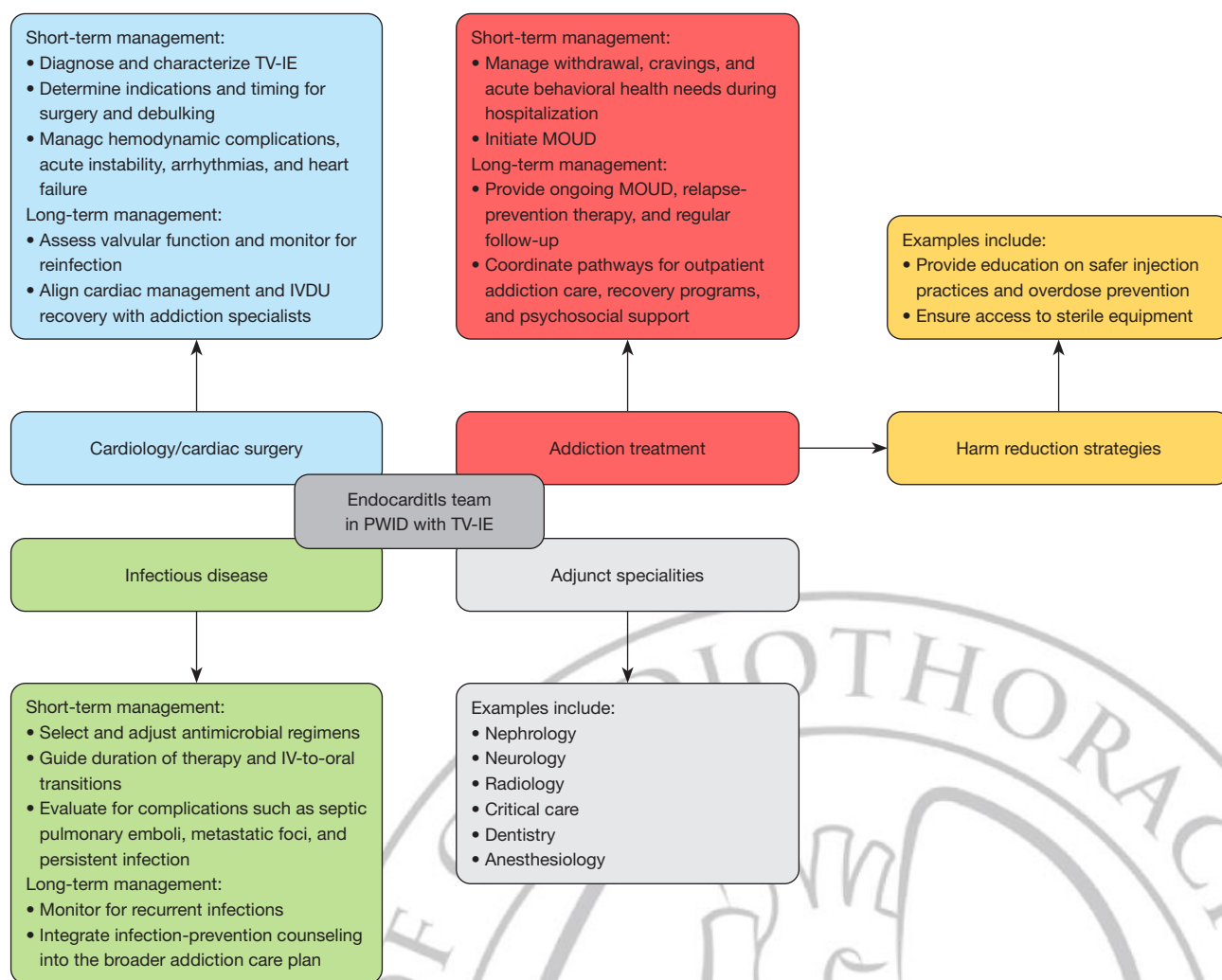


Figure 1 Concept of a multidisciplinary Endocarditis Team for the management of tricuspid valve infective endocarditis in people who inject drugs. IVDU, intravenous drug use; MOUD, medications for opioid use disorder; PWID, people who inject drugs; TV-IE, tricuspid valve infective endocarditis.

health support and social work, is critical for promoting adherence and stability. Systematic assessment of social determinants of health, including housing stability, access to addiction treatment, and social support, may further help identify barriers to successful treatment and should be considered as part of comprehensive multidisciplinary care. In selected patients, long-acting antibiotics or evidence-based oral step-down regimens may offer additional support for continuity of care. Further, screening for infections commonly associated with injection drug use, testing for human immunodeficiency virus (HIV) and hepatitis B and

C, and vaccination for tetanus, hepatitis B, and hepatitis A when appropriate are essential components of follow-up care.

As patients improve clinically, the inpatient team should identify an appropriate and safe setting for post-acute care, considering the patient's preferences as well as practical considerations such as distance, financial constraints, and available social support.

When abstinence is not immediately achievable, harm-reduction strategies including access to sterile supplies, supervised consumption sites, and education on safer

injection techniques are essential to reducing reinfection risk and improving patient safety.

In summary, during the acute hospitalization phase, cardiology and cardiac surgery as well as infectious disease management play the predominant role in stabilizing the patient, eradicating infection, and determining the need for operative intervention. As time progresses beyond discharge, the prognostic influence of these acute-care specialties gradually declines. Addiction treatment, harm-reduction strategies, and longitudinal management of substance use disorder become essential to reduce reinfection, recurrent hospitalizations, and late mortality, and are the major determinants of long-term outcomes.

Conclusions

IVDU-associated TV-IE represents a complex intersection of infectious disease, structural heart disease, substance use, and social vulnerability. Although most cases can be managed medically, outcomes remain limited by high rates of reinfection, patient-directed discharge, and challenges in completing antimicrobial therapy. Surgical intervention plays an important role in selected patients. Long-term survival is often compromised by ongoing IVDU rather than being directly related to acute TV-IE. Meaningful improvement in outcomes requires a comprehensive model of care that integrates optimized antimicrobial and surgical therapy, early and sustained engagement in addiction treatment, and robust harm-reduction strategies. Coordinated multidisciplinary follow-up, behavioral health support, and attention to housing and social stability are essential to reducing recurrent infection and improving long-term recovery. Ultimately, strategies that combine evidence-based clinical management with public health interventions targeting substance use and its determinants offer the best opportunity to reduce mortality and recurrence and improve the lives of individuals affected by IVDU-associated TV-IE.

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