

The Infectious Tricuspid Endocarditis in ICU: Clinical Features, Management and Outcome

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Abstract: Objectives: Infectious tricuspid endocarditis is known to simply require antibiotherapy and to have good prognosis in most cases. Few studies focused on severe episodes managed in ICU. We aimed to describe clinical and microbiological features, and final outcome of infectious tricuspid endocarditis managed in ICU. Methods: From 1 January 2009 to 31 August 2017, all patients hospitalized in intensive care unit with infectious tricuspid endocarditis were enrolled. Key findings: We collected 15 episodes of infectious tricuspid endocarditis. Median age was of 39 years. Risk factors were: intravenous drug users (n = 10), pace maker (n = 1), vascular device (n = 2), none (n = 2). Median SAPS II, APACHE II and SOFA on admission were 21, 10 and 2 respectively. Organ failures on admission were: acute respiratory failure (n = 10), sepsis (n = 7), coma (n = 1) and acute kidney injury (n = 8). The most frequent causative pathogen was *Staphylococcus Aureus*. Antibiotherapy failure happened in 10 patients from whom 8 underwent cardiac surgery (53.3%). Most frequent complications were acute kidney injury (n = 14) and withdrawal syndrom. Infectious tricuspid endocarditis relapse on bioprosthesis occurred within 2 intravenous drug users after hospital discharge. Overall in-hospital mortality was 40%. Conclusions: Infectious tricuspid endocarditis in ICU is fitted with poor prognosis and high need to cardiac surgery. Special care should be provided to intravenous drug users to prevent relapse.

Key words: Infectious endocarditis, tricuspid valve, intensive care unit, intravenous drug users, *staphylococcus aureus*, complications, surgery, endocarditis recurrence, withdrawal syndrome.

1. Introduction

Right-sided infective endocarditis accounts for only 5%-10 % of cases of infective endocarditis [1]. Tricuspid valve is the most frequent location. It especially occurs among IDUs (intravenous drug users) or after intravascular devices need [2].

The prognosis of native valve right sided endocarditis is known to be favorable. Nevertheless, these patients may need to be managed in intensive care units when complications occur and lead to one or several organ failures. Although management and mortality predictors were widely studied in left-sided infectious endocarditis, many grey areas remain concerning right-sided infectious endocarditis, especially about surgical requirement, outcome

predictors and long-term imperative needs. That's why reporting experiences worldwide is essential to build consensual short and long-term management for severe right-sided infectious endocarditis.

This study focused on ITE (infectious tricuspid endocarditis) managed in ICU (intensive care unit) and aimed to describe the clinical and microbiological features, risk factors, medical and surgical treatments, and final outcome.

2. Methods

2.1 ICU Presentation

Our unit is a 22 bed medical ICU with a respiratory valence. It belongs to a teaching university hospital of pneumology (301 beds): Abderrahmen Mami hospital of Ariana, Tunisia. The mean number of ICU admissions is about 545 per year.

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2.2 Study Design and Patients

We conducted a retrospective observational cohort study using prospectively collected data over an 8-year and 8-month period (from 1 January 2009 to 31 August 2017).

We enrolled all patients hospitalized in ICU for ITE according to modified Duke criteria [3].

2.3 Data Collection

In all patients, we recorded socio-demographic data: age, gender and history of incarceration. We also noticed risk factors for ITE: intravenous drug addiction, pacemakers and vascular devices.

Initial severity was assessed by SAPS II, APACHE II and SOFA scores at admission and we listed organ dysfunctions.

Echocardiographic findings and microbiological specificities of blood culture results were detailed. Global management, complications, ICU mortality and ICU length of stay were also recorded. Statistical analysis was performed by SPSS soft-ware package and data were expressed with absolute and relative frequencies.

2.4 Definitions

ARDS: acute respiratory distress syndrome (the Berlin definition) [4].

➤ Timing: Within 1 week of a known clinical insult or new or worsening respiratory symptoms;

➤ Chest imaging: Bilateral opacities, not fully explained by effusions, lobar/lung collapse, or nodules, observed on chest radiograph or computed tomography scan;

➤ Edema origin: Respiratory failure not fully explained by cardiac failure or fluid overload, with the need for objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor is present;

➤ Oxygenation:

• Mild ARDS: $200 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 < 300 \text{ mmHg}$ with PEEP or $\text{CPAP} \geq 5 \text{ cm H}_2\text{O}$;

• Moderate ARDS: $100 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 < 200 \text{ mmHg}$ with $\text{PEEP} \geq 5 \text{ cm H}_2\text{O}$;

• Severe ARDS: $\text{PaO}_2/\text{FiO}_2 < 100 \text{ mmHg}$ with $\text{PEEP} \geq 5 \text{ cm H}_2\text{O}$.

Paraclinical explorations: transthoracic echocardiography, transoesophageal echocardiography, chest computed scan, abdominal echography, abdominal scan, bronchial fibroscopy, thoracic echography and vascular Doppler ultrasound.

Antibiotic failure: need for cardiac surgery or death of the patient before surgery.

3. Results

During the study period, we collected 15 episodes of ITE with an incidence of 3 cases for 1000 patients ICU admissions. They were 13 men and 2 women.

The median age was of 39 years (24-77). Patients' characteristics are summarized in Table 1.

On admission, all patients had serious organ dysfunctions (respiratory, hemodynamic, neurologic and metabolic). Severity criteria are listed in Table 2.

Paraclinical findings:

TTE (Transthoracic echocardiography) was performed in all patients ($n = 15$) and TOE (transoesophageal echocardiography) was necessary in 9 patients. Tricuspid location was exclusive in 14 cases and mitral vegetation was associated in one case. Multiple

Table 1 Patients characteristics of ITE patients admitted in ICU.

	N (%)
Underlying heart disease	0
ITE risk factors	
IDUs	10 (66.7)
Pace maker	1 (6.7)
Central vascular device	2 (13.3)
None	2 (13.3)
HIV	0
Hepatitis C	5 (33.3)
Diabetes mellitus	3 (20)
Tuberculosis	2 (13.3)
Incarceration history	3 (20)

ITE: infectious tricuspid endocarditis; ICU: intensive care unit; IDUs: intravenous drug users; HIV: human immunodeficiency virus.

Table 2 Severity criteria on admission.

SAPS II, med. ± SD	21 ± 10.3
APACHE II, med. ± SD	10 ± 5.3
SOFA, med. ± SD	2 ± 2.5
ARF, n (%)	10 (66.7)
ARDS mild n (%)	1 (6.7)
ARDS moderate n (%)	3 (20)
ARDS severe n (%)	2 (13.3)
Sepsis n (%)	7 (46.7)
Coma n (%)	1 (6.7)
AKI n (%)	8 (53.3)

SAPS II: Simplified acute physiology score II; APACHE II: Acute physiology and chronic health evaluation; SOFA: Sequential organ failure assessment; ARF: acute respiratory failure, ARDS: acute respiratory distress syndrome, AKI: acute kidney injury/impairment.

vegetations were individualized in 6 patients. The median size of vegetations was 18.8 ± 5.3 mm (9-28). Acute cor pulmonale was recorded in one patient.

Patients undergone several paraclinical explorations (median=5, (1-14)) to determine different septic localizations of ITE: pulmonary parenchyma (n = 12), lung septic emboli (n = 7), pleural effusions (n = 8) and renal abscess (n = 2).

Causative pathogens were identified in 13 patients having positive blood cultures. They were dominated by *Staphylococcus aureus*. Polymicrobial infection was observed in 3 patients. Pathogens types and frequencies are listed in Table 3.

Empiric antibiotherapy was prescribed for all patients according to guidelines, then adapted to blood cultures' results. Most used antibiotics are shown in Fig. 1.

Table 3 Blood cultures findings.

	N (%)
<i>Staphylococcus aureus</i>	9 (60)
MRSA	6 (40)
MSSA	3 (20)
<i>Coagulase-negative staphylococcus</i>	2 (13.3)
Enterococcus	1 (6.7)
<i>Enterobacter cloacae</i>	1 (6.7)
<i>Klebsiella pneumoniae</i>	2 (13.3)
Candida	2 (13.3)
Polymicrobial blood cultures	3 (20)
Negative blood cultures	2 (13.3)

MRSA: Methicillin Resistant *Staphylococcus aureus*; MSSA: Methicillin Sensitive *Staphylococcus aureus*.

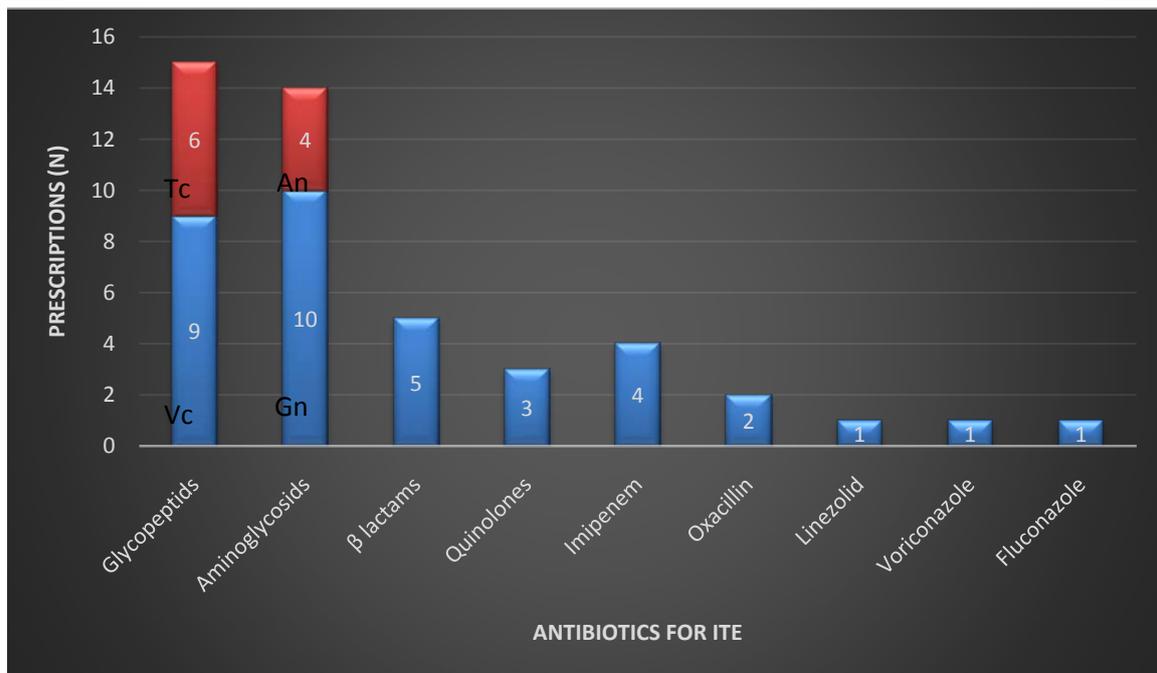


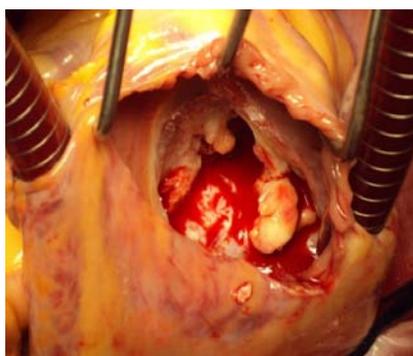
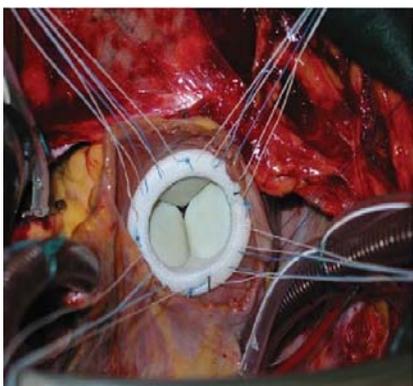
Fig. 1 Different antibiotics used to treat ITE.

Vc: Vancomycin; Tc: teicoplanin; Gn: Gentamicin; An: Amikacin; ITE: Infective tricuspid endocarditis.

Table 4 Early and late complications.

	N (%)
Antibiotherapy failure	10 (66.7)
Hospital-acquired infections	5 (33.3)
Septic shock	3 (20)
Cardiac arrest	2 (13.3)
Atrioventricular block	2 (13.3)
AKI	14 (93.3)
Withdrawal syndrome	7 (46.6)
Drug addiction recurrence	3 (20)
ITE recurrence	2 (13.3)

AKI: acute kidney injury/impairment, ITE: infective tricuspid endocarditis.

**Fig. 2a Vegetations on tricuspid valves.****Fig. 2b Resected valve.****Fig. 2c Bovine prosthesis replacement.****Table 5 Therapeutic and outcome findings.**

	Mean \pm SD	Extremes
Days with vasopressors (n = 8, 53.3%)	1.67 \pm 2.4	1-8
Days with catheters (n = 9, 60%)	5.9 \pm 13.1	1-49
Days with MV (n = 15, 100%)		
- IV (n = 9, 60%)	5.1 \pm 7.9	1-23
- NIV (n = 6, 40%)		
Days with antibiotics (n = 15, 100%)	20.3 \pm 15.8	1-56
Length of stay, days	25.5 \pm 20.3	1-59

MV: Mechanical Ventilation; IV: Invasive Ventilation; NIV: Non Invasive Ventilation; SD: standard deviation.

In hospital mortality was of 40%. The outcome was favorable in 9 patients and 6 patients died from shock and multiorgan failure.

Mortality within IDUs (n = 10) was of 50% (n = 5). Mortality within IDUs operated (n = 7) was of 57% (n = 4).

Many complications occurred during ICU stay. Withdrawal syndrome was the main complication observed in all IDUs (tachycardia, fever, agitation) treated by Clonidine and Chlorpromazine. Successfully discharged patients were then regularly followed up and further complications were recorded. Main of these early and late complications are listed in Table 4.

Surgical treatment was necessary in 8 patients from whom 7 were IDUs: tricuspid valve replacement by bioprosthesis device (6 cases) (Figs. 2a, 2b and 2c) and repairs by valve reconstruction (2 cases). Decision criteria were: vegetations' size growing in spite of well conducted and adaptive antibiotherapy (n = 4), non-controlled sepsis (n = 3) and mechanical complication with massive tricuspid regurgitation (n = 1).

Two patients recurred ITE on bioprosthesis devices because of intravenous drug resumption after discharge, they underwent surgery again and one of them died.

Therapeutic and outcome findings are given in Table 5.

4. Discussion

This study showcases severe forms of ITE with multiple extra cardiac locations (pulmonary, pleural and renal) and main life-threatening distresses

(respiratory, hemodynamic, neurologic and metabolic). They required both medical and surgical management enameled with several complications. Heavy burden based on mechanical ventilation, renal replacement therapy, vasopressors and central vascular catheterization was necessary. After long length of stay, final outcome was poor.

ITE is known to be benign and fitted with good prognosis [2]. Reported in-hospital mortality within right-sided infective endocarditis is approximately 7% [5]. Nevertheless, very few studies focused on management and outcome of ITE with severe organ failures that needs admission to ICU.

In 2001, Wolff [6] reviewed 127 serious infectious endocarditis in ICU including 21 right-sided IE (17 IDUs) with an in-hospital mortality of 33%. He highlighted the important rate of deaths related to sepsis severity within these patients. In 2010, Saydain et al. [7] aimed to study the outcome of IDUs presenting with complicated infective endocarditis, both right- and left-sided admitted to an ICU. Among 33 IDUs patients, higher mortality (27%) than previously reported was noticed. In 2016, mortality reported in a small Indian cohort of 11 ICU patients IDUs having right-sided endocarditis was of 9% [8]. In 2017, Wilson et al. [9] retrospectively reviewed 53 IDUs admitted to ICU from whom 30 (56.6%) had acute infective bacterial endocarditis: these patients demonstrated a high need to critical care resources, especially mechanical ventilation.

Our study described a subgroup of ITE with many extra cardiac damages leading to a high level of initial severity. These patients needed organ support therapy: mechanical ventilation in all cases and surgery in half cases. Mortality was high reaching 40%. This severity could be explained by the "tricuspid syndrome" or multiple organ implication which is possibly due to circulating immune complex deposition rather than septic emboli [10]. In 2016, a 105-patient cohort study focused on predictors of outcome in right-sided infectious endocarditis. Patients who died were

significantly more likely to require ICU admission, mechanical ventilation and new hemodialysis support. After multiple regression models, immunosuppression, elevated blood urea nitrogen and presence of right ventricle systolic dysfunction were significantly correlated with in-hospital mortality [11].

Usually, most cases of right-sided IE resolve simply with appropriate antibiotic without need of further surgical management [2]. In our study, surgical treatment was necessary in 8 patients (53.3%). It is worth considering main reasons leading to such high rate of medical treatment failure and need to cardiac surgery. First, we supposed that antibiotic failure was probably due to delay on diagnosis and treatment. Clinical presentation made of febrile pneumonia in young patients is often considered as a banal pulmonary infection while septic emboli are already sent to lungs. In 2014, Chang-Esaki et al. [12] validated a prediction rule based on 3 clinical findings which combine tachycardia, cardiac murmur and absence of skin infection. In emergency department, this instrument predicted infectious endocarditis among febrile IDUs with high sensitivity and ruled out it with high negative predictive value.

Second, 7 patients were IDUs and had pulmonary septic locations. Liu S. et al [13] studied clinical course of 34 patients with septic pulmonary embolism caused by right-sided infective endocarditis and reported cardiac surgery need of 76.5%. Third, identified pathogens among surgical patients were *Staphylococcus aureus* in 7 cases and *Klebsiella pneumoniae* in 1 case. Spreading and adhesion power of *Staphylococcus aureus* are already well established and may predict resistance to antibiotics, even well conducted. In fact, *Staphylococcus aureus* has been found to be associated with high complication rates including extra cardiac deep infections, thromboembolic events or severe sepsis in IDUs infective endocarditis [14].

In our country, we are witnessing an outbreak scourge of intravenous drug addiction that is not easily

measurable nor confessed. In Tunisia, there is a unique addiction treatment center run by a non-governmental organization. A recent Tunisian study described drug users that requested this center: they were 202 patients between January 2014 and September 2014 from whom 39% (n = 78) were IDUs and frequently shared their needles [15]. In our study, drug addiction recurrence after hospital discharge was noted in 3 patients among the 5 IDUs discharged; 2 of them retrieved ITE. In 2016, a cohort of 38 IDUs with isolated ITE was reviewed to evaluate the incidence of death in two years from the diagnosis; the highest risk for mortality appears to be ongoing intravenous drug using and persistent or recurrent endocarditis [16]. Hence, drug addiction weaning should be a cornerstone of the management of ITE among IDUs. Unfortunately, huge efforts should be deployed to diagnose, treat and prevent addiction to illicit drugs, which is a worldwide health problem involving about 5% of the world's adult population [17].

5. Conclusions

The ITE in ICU is a severe disease with frequent extra-cardiac complications and high in-hospital mortality. The most frequent incriminated pathogen is *Methicillin resistant Staphylococcus aureus*. It often requires medical and surgical treatment in addition to organ supply techniques. Cardiac surgery need was associated to septic lung complications and *Staphylococcus aureus*. Intravenous drug addiction remains the most common cause and worsens the prognosis by the risk of recurrence. Multi-center findings should be collected to analyze outcome according to management patterns, so that official guidelines for severe right-sided infectious endocarditis could be accurately established.

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Declarations of Interest

The authors declare no conflict of interest.

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