

# Chapter 70

## Approach to Infective Endocarditis in the ICU



### 70.1 Introduction

Infective endocarditis (IE) is a severe, life-threatening infection of the endocardial surface of the heart, primarily affecting the heart valves. IE in the intensive care unit (ICU) often presents with diagnostic ambiguity, frequently mimicking other systemic infections. Early bedside suspicion and coordination with microbiology and cardiology teams are essential. Risk factors include prosthetic heart valves, previous history of endocarditis, intravenous drug use, immunosuppression, and recent healthcare exposure. Early recognition and initiation of appropriate diagnostics and treatment are essential for improving patient outcomes. This chapter provides ICU clinicians with a structured approach for assessing and managing suspected infective endocarditis [1, 2] [Ref: Algorithm 70.1].

### 70.2 Diagnosis Initial Suspicion

- Clinical Features: IE may present with a variety of symptoms, including fever, new or changing heart murmurs, embolic events (e.g., stroke, limb ischemia), sepsis, and peripheral manifestations like Janeway lesions, Osler nodes, Roth spots, or splinter hemorrhages. These findings should raise suspicion, particularly if multiple features are present.
- Risk Factors: Patients with prosthetic heart valves, previous endocarditis, and congenital heart disease, a history of intravenous drug use, immunosuppression, or recent healthcare exposure (such as surgery or invasive procedures) are at heightened risk. Awareness of these risk factors can prompt early evaluation for IE.

- Microbial Shifts: There is an increased prevalence of healthcare-associated infections with methicillin-resistant *Staphylococcus aureus* (MRSA) and other resistant pathogens, reflecting current epidemiological trends. This shift necessitates vigilance in both diagnosis and empirical therapy selection.

## 1. Suspicion for Infective Endocarditis

- Assess the likelihood of IE based on clinical presentation and risk factors. If IE is not considered likely, evaluate other possible causes of the symptoms, such as other infectious or inflammatory conditions.

## 2. Diagnostic Evaluation

- Blood Cultures: Obtain at least three separate blood cultures from different venipuncture sites before initiating antibiotics with the first and last samples drawn at least 1 hour apart. In cases of suspected blood culture-negative endocarditis, consider serological and molecular diagnostic techniques to detect fastidious organisms like *Coxiella burnetii* or *Bartonella* species.
- Echocardiography:
- Transthoracic Echocardiography (TTE): Initiate diagnostic imaging with TTE, which is noninvasive and can provide initial evidence of vegetations, abscesses, or valve dysfunction.
- Transesophageal Echocardiography (TEE): If TTE is inconclusive or if the patient has prosthetic valves, TEE should be performed due to its higher sensitivity and specificity.
- Advanced Imaging Techniques: In cases where TEE is inconclusive or in prosthetic valve endocarditis, consider advanced imaging modalities like positron emission tomography-computed tomography (PET-CT) or cardiac magnetic resonance imaging (MRI). These techniques can detect occult infections and embolic phenomena.

### **70.2.1 Modified Duke Criteria: Clinical Framework for Diagnosing Infective Endocarditis**

The Modified Duke Criteria provide a structured, evidence-based method to support the diagnosis of infective endocarditis by integrating clinical features, microbiological data, and imaging findings.

#### 1. Definite Infective Endocarditis

- Pathological Confirmation: Diagnosis is established when microorganisms are directly isolated from cardiac tissue, such as vegetations or abscesses, through culture or histological examination. Alternatively, microscopic features consistent with endocarditis in excised cardiac material also fulfill this criterion.

- Clinical Combination-Based Diagnosis: Can be made when any of the following are met:

- Two major criteria
- One major and three minor criteria
- Five minor criteria

## 2. Possible Infective Endocarditis

- Supported by:
- One major and one minor criterion
- Three minor criteria

## 3. Major Diagnostic Criteria

- Microbiological evidence:
  - Two or more blood cultures positive for typical IE pathogens
  - A single positive culture or high-titer serology (e.g., *Coxiella burnetii* with anti-phase I IgG  $\geq 1:800$ ) also qualifies
- Evidence of endocardial involvement:
  - Findings on echocardiography include:
    - Mobile intracardiac mass attached to valves, supporting structures, or device leads
    - Perivalvular abscess formation
    - Prosthetic valve dehiscence
    - Newly developed valvular regurgitation (excluding simple murmur changes)

## 4. Minor Diagnostic Criteria

- Presence of known cardiac abnormalities or IV drug use
- Temperature  $\geq 38^{\circ}\text{C}$
- Vascular complications such as emboli, infarcts, aneurysms, or peripheral lesions (e.g., Janeway)
- Immunological signs like Osler nodes, Roth spots, glomerulonephritis, or positive rheumatoid factor
- Microbiological findings that don't fulfill major criteria (e.g., single positive culture or atypical)

## 70.3 Management

### 70.3.1 Empirical Therapy (Table 70.1)

Empiric antibiotic therapy generally includes intravenous vancomycin combined with ceftriaxone or ampicillin to cover common organisms like *Staphylococcus*, *Streptococcus*, and *Enterococcus* species (Table 70.1 and 70.2).

**Table 70.1** Native Valve Endocarditis

Organism	Antibiotic	Dose	Duration	Remarks
Viridans streptococci or <i>streptococcus gallolyticus</i> strains with confirmed sensitivity to penicillin	Ceftriaxone or Penicillin G or Ampicillin or Ceftriaxone + gentamicin or Vancomycin	2 g IV once daily Penicillin G at 12 to 18 million units daily, infused continuously or intermittently in 4 to 6 divided doses A total of 12 grams per day administered intravenously in 4 to 6 separate doses Ceftriaxone 2 grams IV once per day combined with gentamicin at 3 mg/kg IV given once daily Administer 30 mg/kg per day intravenously, divided into 2 doses	4 weeks	
Viridans streptococci and <i>S. Gallolyticus</i> strains demonstrating intermediate or reduced susceptibility to penicillin	Penicillin G + Gentamicin	24 million U IV in 4–6 equally divided doses +3 mg/kg IV once daily	Penicillin 4 weeks Gentamicin 2 weeks	Use ceftriaxone if ceftriaxone sensitive
	Ampicillin + gentamicin	12 g/day IV in 4–6 divided doses +3 mg/kg IV once daily	Ampicillin 4 weeks + gentamicin 2 weeks	
	Vancomycin	30 mg/kg IV in 2 divided doses	4 weeks	Only for patients unable to tolerate penicillin or ceftriaxone

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**Table 70.1** (continued)

Organism	Antibiotic	Dose	Duration	Remarks
Enterococcus	Penicillin G + gentamicin Or	18–30 million U IV in 4–6 equally divided doses +3 mg/kg IV in 3 divided doses	4–6 weeks	When symptoms have been present for less than 3 months, a 4-week antibiotic regimen is advised; if symptoms exceed 3 months, a 6-week duration is recommended for native valve endocarditis
	Ampicillin Or	Administer a total of 12 grams per day intravenously, divided into 4 to 6 doses	4–6 weeks	Same as above
	Vancomycin + gentamicin Or	Administer vancomycin 30 mg/kg per day intravenously in 2 doses, along with gentamicin 3 mg/kg per day IV split into 3 equal administrations	6 weeks	Beta-lactamase producer
	Ampicillin + ceftriaxone	Administer ampicillin 2 grams intravenously every 4 hours, along with an additional ceftriaxone 2 grams IV every 12 hours	6 weeks	In renal failure who can't tolerate gentamicin
	Linezolid	Administer 600 mg either intravenously or orally every 12 hours	6 weeks	In cases where the pathogen exhibits resistance to penicillin, aminoglycosides, and vancomycin
Staphylococci	Nafcillin or oxacillin (sensitive)	Administer a total of 12 grams intravenously over 24 hours, divided into 4 to 6 equal doses	6 weeks	A full treatment course is required for left-sided endocarditis and complicated right-sided cases, while a shorter 2-week regimen may be sufficient for uncomplicated right-sided infections

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**Table 70.1** (continued)

Organism	Antibiotic	Dose	Duration	Remarks
	Cefazolin	Administer a total of 6 grams intravenously per day, split into 3 equal doses	6 weeks	
	Vancomycin	Administer 30 mg per kg of body weight per day, split into 2 equal intravenous doses	6 weeks	
	Daptomycin	At least 8 mg per kg per dose	6 weeks	
HACEK	Ceftriaxone or	2 g IV once daily	4 weeks	
	Ampicillin or	12 g/day IV in 4–6 divided doses		
	Ciprofloxacin	400 mg IV twice daily or 500 mg orally twice daily	6 weeks	If unable to tolerate cephalosporin
Non-HACEK gram-negative	Penicillin G/ampicillin/ceftriaxone/carbapenem + gentamicin/ciprofloxacin			Along with surgery
Fungal	Amphotericin B followed by lifelong oral azole		6 weeks	Along with surgery

### 70.3.2 Prognostic Scoring and Risk Assessment

- EuroSCORE II: Incorporate prognostic tools like EuroSCORE II at admission to assess surgical risk and aid in decision-making. This scoring system evaluates factors such as patient age, comorbidities, and hemodynamic status to predict operative mortality.

### 70.3.3 Clinical Stability

- Assessment: Monitor the patient's response to empirical therapy, focusing on fever resolution, hemodynamic stability, and symptom progression.

**Table 70.2** Prosthetic valve endocarditis

Organism	Antibiotic	Dose	Duration	Remarks
Viridans group streptococci and <i>streptococcus gallolyticus</i> strains confirmed to be sensitive to penicillin	Ceftriaxone ± gentamicin or	Ceftriaxone 2 g IV once daily, with or without gentamicin at 3 mg/kg per day administered as a single IV or IM dose	Ceftriaxone 6 weeks Gentamicin 2 weeks	Extend gentamicin therapy to 6 weeks when the minimum inhibitory concentration (MIC) exceeds 0.12 µg/mL for the identified pathogen
	Penicillin G or	Penicillin G at a total daily dose of 24 million units, administered intravenously either as a continuous infusion or in 4 to 6 evenly spaced doses	6 weeks	
	Vancomycin or	Vancomycin at a total daily dose of 30 mg/kg IV, administered in 2 equal doses over 24 hours	6 weeks	
	Ampicillin	Administer ampicillin 2 grams intravenously every 4 hours	6 weeks	
Strains of VGS and <i>S. Gallolyticus</i> exhibiting partial resistance to penicillin	Ceftriaxone + gentamicin or	Ceftriaxone 2 g IV once daily combined with gentamicin 3 mg/kg per day, administered as a single IV or IM dose	Ceftriaxone 6 weeks Gentamicin 2 weeks	Extend gentamicin therapy to 6 weeks when the minimum inhibitory concentration (MIC) exceeds 0.12 µg/mL for the identified pathogen
	Vancomycin or	30 mg/kg per 24 h IV in 2 equally divided doses	6 weeks	
	Ampicillin	2 g IV every 4 h	6 weeks	
Staphylococci	Nafcillin or oxacillin (sensitive) + rifampin + gentamicin	2 g/24 h IV in 4–6 equally divided doses + 900 mg per 24 h IV or orally in 3 equally divided doses + 3 mg/kg per 24 h IV or IM in 2 or 3 equally divided doses	Oxacillin ≥6 weeks Rifampin ≥6 weeks Gentamicin 2 weeks	If oxacillin sensitive

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**Table 70.2** (continued)

Organism	Antibiotic	Dose	Duration	Remarks
	Vancomycin + rifampin + gentamicin	30 mg/kg 24 h in 2 equally divided doses + 900 mg per 24 h IV or orally in 3 equally divided doses + 3 mg/kg per 24 h IV or IM in 2 or 3 equally divided doses	≥6 weeks	If oxacillin resistant, maintain trough concentration of 10–20 µg/mL. Rifampin is included to target biofilm-associated pathogens on prosthetic material
Enterococci		Same as native valve endocarditis (usually always 6 weeks)		
HACEK		Same as native valve endocarditis (duration of therapy: 6 weeks)		
Non-HACEK gram-negative		Same as native valve endocarditis (antibiotics + surgery)		
Fungal		Same as native valve endocarditis (amphotericin B + surgery)		

- Stable Patients: If the patient is clinically stable, continue antimicrobial therapy tailored to culture results and monitor for complications.
- Unstable Patients: If the patient remains unstable or deteriorates, proceed to urgent multidisciplinary evaluation.

#### **70.3.4 Multidisciplinary Care and Cardiothoracic Surgery Review**

- Endocarditis Team: Establish a dedicated “Endocarditis Team” involving infectious disease specialists, cardiologists, cardiac surgeons, microbiologists, and other relevant experts. This team approach has been shown to improve patient outcomes.
- Surgical Timing and Indications:
  - Persistent Bacteremia: Ongoing bacteremia despite adequate antibiotic therapy suggests uncontrolled infection requiring surgical intervention.
  - Valve Dysfunction: Severe valve dysfunction leading to heart failure may necessitate urgent valve repair or replacement.
  - Large Vegetations: Vegetations larger than 10 mm, especially those with prior embolic events, increase the risk of further embolism.
  - Abscess Formation or Fungal Infection: Intracardiac abscesses and fungal endocarditis often require surgical debridement due to poor response to medical therapy alone.
  - Neurological Complications: Careful timing of surgery is critical in patients with recent cerebral emboli or hemorrhage; collaboration with neurologists is essential [3].

### ***70.3.5 Management of Complications***

Neurological:

- Embolic Stroke: Implement neuroimaging if neurological signs arise. Manage strokes according to standard protocols, considering the risks and benefits of anticoagulation.
- Mycotic Aneurysms: Monitor for cerebral mycotic aneurysms, which may require neurosurgical intervention.

Cardiac:

- Heart Failure: Optimize medical management and consider mechanical support if necessary.
- Arrhythmias: Monitor and treat arrhythmias promptly.

Systemic Embolism:

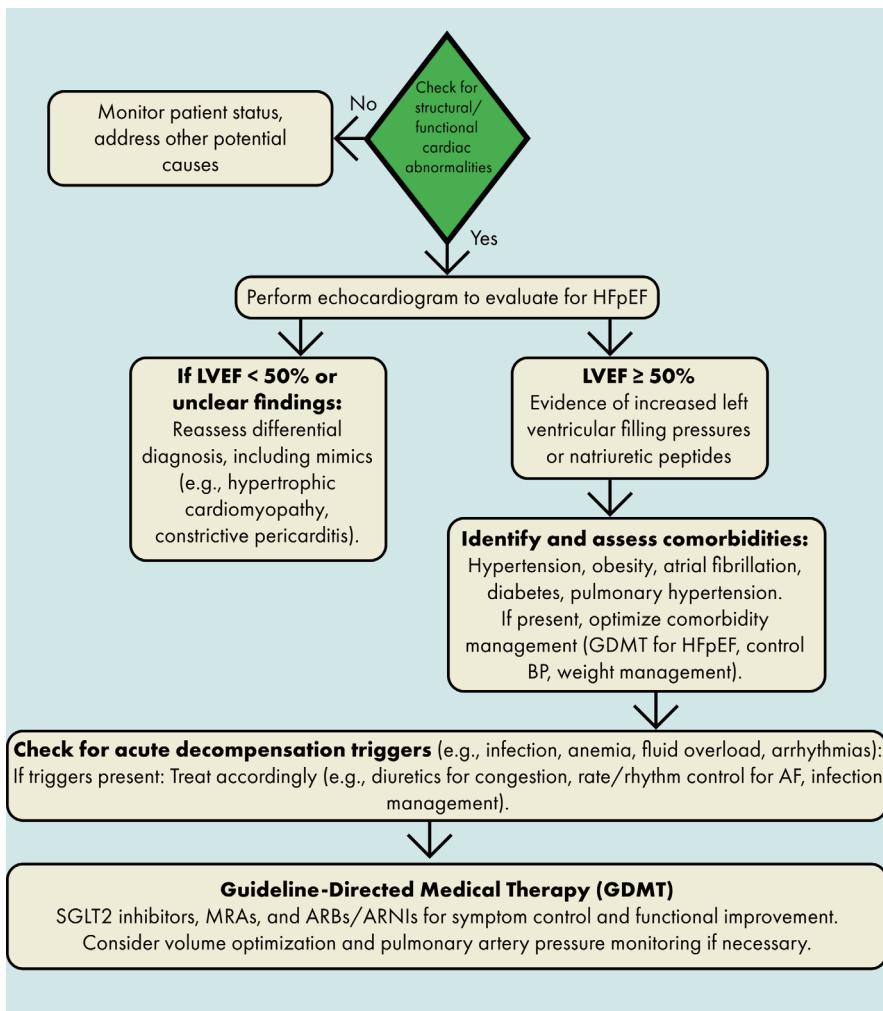
- Splenic Abscess: Suspect in patients with left upper quadrant pain; management may include antibiotics and possible surgical intervention.
- Renal Infarction: Monitor renal function and manage accordingly.
- Peripheral Emboli: Assess limbs for ischemia; surgical or endovascular interventions may be required.

## **70.4 Emerging Evidence and Research Trends**

- Minimally Invasive Surgical Techniques: Research into less invasive surgical options aims to reduce operative risk and improve recovery times.
- Molecular Diagnostics: Advances in molecular techniques may enhance the detection of fastidious organisms and guide more precise antimicrobial therapy.

## **70.5 Conclusion**

The management of infective endocarditis in the ICU is complex and requires a multidisciplinary, systematic approach for diagnosis, treatment, and prevention of complications. Early recognition, comprehensive diagnostic evaluation—including advanced imaging and microbiological techniques—and prompt initiation of appropriate antimicrobial therapy are crucial. The involvement of an Endocarditis Team facilitates coordinated care, optimizing both medical and surgical interventions. By integrating prognostic assessments, patient-centered education, and awareness of emerging evidence, ICU clinicians can significantly improve patient outcomes in this challenging condition.

**Algorithm 70.1: Approach to infective endocarditis in the ICU**

## Bibliography

1. Delgado V, Ajmone Marsan N, de Waha S, Bonaros N, Brida M, Burri H, et al. ESC guidelines for the management of endocarditis. *Eur Heart J.* 2023;44(39):3948–4042.
2. McDonald EG, Aggrey G, Tarik Aslan A, Casias M, Cortes-Penfield N, Dong MQD, et al. Guidelines for diagnosis and management of infective endocarditis in adults: a WikiGuidelines group consensus statement. *JAMA Netw Open.* 2023;6(7):e2326366.
3. Baddour LM, Wilson WR, Bayer AS, Fowler VG Jr, Tleyjeh IM, Rybak MJ, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and Management of Complications: a scientific statement for healthcare professionals from the American Heart Association. *Circulation.* 2015;132(15):1435–86.