RESEARCH PORTAL CENTRAL

Journal of Surgical Case Reports and Research

OPEN ACCESS

Review Article

Surgical Timing in Infective Endocarditis: Determinants and Clinical Implications

Running Title: Timing of Surgery in Endocarditis

Ömer Burak Çelik[1], Macit Kalçik[2]*, Abdullah Sarihan[3], Oğuzhan Çelik[4], Mehmet Mustafa Yilmaz[1], Osman Karaarslan[1], Mucahit Yetim[2], Muhammet Cihat Çelik[1], Lütfü Bekar[2], Yusuf Karavelioğlu[2]

1. Department of Cardiology, Hitit University Erol Olçok Education and Research Hospital, Corum, Turkey.
2. Department of Cardiology, Faculty of Medicine, Hitit University, Corum, Turkey.
3. Department of Cardiology, Faculty of Medicine, Muğla University, Muğla, Turkey.
4. Department of Cardiology, Gediz State Hospital, Kütahya, Turkey.

How to cite this article: Ömer B. Çelik, M. Kalçik, A. Sarihan, O. Çelik, Mehmet M. Yilmaz, et al. (2026). Surgical Timing in Infective Endocarditis: Determinants and Clinical Implications. *Journal of Surgical Case Reports and Research*, 2(1); DOI: https://www.doi.org/rpc/2026/jscrr/00539

***Address for correspondence:** Macit Kalçik, Department of Cardiology, Faculty of Medicine, Hitit University, Corum, Turkey.
Email: macitkalcik@yahoo.com

Submitted: March 03, 2026
Approved: April 02, 2026
Published: April 10, 2026

Abstract

Infective endocarditis remains associated with substantial morbidity and mortality despite advances in antimicrobial therapy and imaging techniques. Surgical intervention is required in nearly half of affected patients; however, determining the optimal timing of surgery continues to represent a major clinical challenge. The decision is influenced not only by infection control but also by the dynamic progression of structural damage, embolic risk, and hemodynamic compromise. Ongoing valvular destruction may lead to acute regurgitation and heart failure, while extension of infection beyond the valve can result in abscess formation or fistulous communication, both of which are associated with poor outcomes if intervention is delayed. Vegetation size, mobility, and location play critical roles in embolic risk stratification, and early surgery may reduce the likelihood of recurrent embolic events in high-risk patients. Neurological complications further complicate decision-making, as ischemic stroke may allow timely intervention in selected cases, whereas intracranial hemorrhage often necessitates postponement. Prosthetic valve involvement represents a particularly aggressive form of disease due to biofilm formation and a higher propensity for perivalvular extension. Optimal management therefore requires integration of clinical status, imaging findings, and neurological assessment. A multidisciplinary approach has emerged as an essential strategy to guide individualized surgical timing and improve outcomes. Early intervention, when appropriately selected, may prevent irreversible structural damage and systemic complications.

Keywords: infective endocarditis; surgical timing; embolic risk; perivalvular complications; multidisciplinary management

Introduction

Infective endocarditis [IE] continues to be associated with considerable morbidity and mortality despite advances in antimicrobial therapy, diagnostic imaging, and perioperative care [1,2]. Contemporary registries indicate that in-hospital mortality remains approximately 15–25%, with one-year mortality approaching 30% in certain subgroups [1]. These unfavorable outcomes are not solely driven by persistent infection but are frequently the consequence of progressive structural damage, embolic complications, and hemodynamic deterioration.

Surgical intervention is required in nearly half of patients diagnosed with IE during the course of their illness [2]. While indications for surgery are generally well established, including heart failure, uncontrolled infection, and prevention of embolic events, the optimal timing of surgical intervention remains a major clinical challenge. In practice, the decision rarely centers on whether surgery is needed, but rather on determining the most appropriate moment to intervene.

Delayed surgery may permit ongoing valve destruction, perivalvular extension of infection, and recurrent embolization, all of which are independently associated with worse outcomes [3]. Conversely, excessively early surgery may carry risks in the presence of neurological complications or uncontrolled sepsis. This balance between urgency and safety represents one of the most complex aspects of IE management.

Accumulating evidence suggests that surgical timing plays a decisive role in modifying prognosis, particularly in patients with high embolic risk, evolving structural damage, or signs of hemodynamic compromise [4]. Therefore, understanding the mechanisms that drive disease progression and the clinical triggers that necessitate early intervention is essential for optimizing patient outcomes.

Pathophysiological Basis for Surgical Timing

The clinical course of infective endocarditis is shaped not only by microbial virulence but also by the dynamic interaction between infection and cardiac structure. Surgical timing is therefore determined by the risk of progressive anatomical damage rather than the presence of persistent bacteremia alone [5].

One of the principal drivers of deterioration is ongoing structural destruction of valvular tissue. Active infection can lead to leaflet perforation, chordal rupture, and loss of coaptation, ultimately resulting in acute regurgitation. Unlike chronic valvular disease, these changes occur rapidly and may precipitate sudden hemodynamic instability. Studies have shown that severe valve dysfunction in IE is frequently associated with early development of heart failure, which is a major predictor of mortality [6].

Another important mechanism influencing surgical timing is the extension of infection beyond the valve leaflets into the surrounding structures. Perivalvular invasion may result in abscess formation, pseudoaneurysm development, or fistulous communication between cardiac chambers. These complications reflect uncontrolled local infection and are strongly associated with poor outcomes if left untreated. Structural complications may evolve even in the setting of microbiological response to antibiotic therapy, underscoring the limitation of relying solely on infection control when deciding the timing of surgery [7].

Embolic potential represents a third pathophysiological component that influences decision making. Vegetations are dynamic structures composed of platelets, fibrin, microorganisms, and inflammatory cells. Their size, mobility, and location determine the likelihood of embolization. Left-sided lesions, particularly those involving the mitral valve, have been associated with higher embolic risk and more severe systemic consequences [8].

Taken together, these mechanisms illustrate that infective endocarditis is not a static disease. The progression of structural damage and embolic risk may continue despite appropriate antimicrobial therapy. Surgical timing must therefore be guided by the anticipated trajectory of anatomical and functional deterioration rather than waiting for complete infection resolution. The principal determinants influencing surgical timing in infective endocarditis are summarized in Table 1.

Table 1: Major Determinants of Surgical Timing in Infective Endocarditis

Determinant	Mechanism	Clinical Consequence	Impact on Timing
Acute valve destruction	Leaflet perforation, chordal rupture	Severe regurgitation → HF	Urgent surgery
Perivalvular extension	Abscess, pseudoaneurysm, fistula	Structural instability	Early surgery
Vegetation characteristics	Large (>10 mm), mobile	High embolic risk	Early surgery
Persistent infection	Biofilm, invasive organisms	Ongoing tissue damage	Early surgery
Hemodynamic compromise	Acute MR / AR, prosthetic dysfunction	Pulmonary edema, shock	Emergency surgery
Neurological complication	Ischemic stroke	Risk–benefit assessment	Individualized
Intracranial hemorrhage	Fragile vascular bed	CPB bleeding risk	Delayed surgery

Abbreviations: *AR: Aortic regurgitation, CPB: Cardiopulmonary bypass, HF: Heart failure, MR: Mitral regurgitation*

Embolic Risk and Surgical Timing

Systemic embolization is one of the most feared complications of infective endocarditis and plays a central role in determining the urgency of surgical intervention. Embolic events occur in a substantial proportion of patients and are most frequent during the early phase of the disease, particularly within the first two weeks after diagnosis [9]. This temporal pattern reflects the heightened instability of vegetations before effective antimicrobial therapy leads to structural consolidation.

The risk of embolization is influenced by several anatomical and clinical factors. Vegetation size has consistently emerged as a strong predictor of embolic events, with lesions exceeding 10 mm associated with a significantly increased risk [10]. In addition to size, mobility is an important determinant of embolic potential. Highly mobile vegetations are more prone to fragmentation and subsequent systemic embolization. The location of infection also contributes to risk stratification, as mitral valve involvement has been linked to higher rates of embolic complications compared to aortic valve infection [11].

Embolization may lead to severe consequences, including ischemic stroke, splenic infarction, renal injury, and peripheral arterial occlusion. Importantly, the occurrence of an initial embolic event substantially increases the likelihood of recurrent embolization. Observational data suggest that early surgical intervention may reduce the incidence of subsequent embolic events in patients with high-risk vegetations [12].

The relationship between neurological complications and surgical timing is complex. While recent ischemic stroke has historically prompted delay in surgical intervention due to concerns regarding hemorrhagic transformation, emerging evidence indicates that early surgery may be safely performed in selected stable patients [13]. Furthermore, silent cerebral emboli are frequently detected on imaging and should not be interpreted as a contraindication to timely surgical management.

These observations support the concept that delaying surgery in patients with high embolic risk does not necessarily confer protection and may instead allow preventable complications to occur. Surgical timing should therefore incorporate individualized assessment of embolic potential rather than relying solely on microbiological response. A structured overview of embolic risk determinants relevant to surgical decision-making is presented in Table 2.

Table 2: Embolic Risk Stratification in Infective Endocarditis

Risk Factor	Associated Findings	Clinical Risk	Surgical Implication
Vegetation >10 mm	Especially >15 mm	High embolic risk	Consider early surgery
High mobility	Oscillating vegetation	Fragmentation risk	Early intervention
Mitral valve location	Anterior leaflet	Cerebral embolism	Lower threshold
Previous embolic event	Stroke, splenic infarct	Recurrence risk ↑	Early surgery
Staphylococcus aureus	Aggressive tissue invasion	Embolic tendency	Early surgery
Multivalvular involvement	Complex infection	Systemic embolization	Early evaluation

Perivalvular Extension and Abscess Formation

Perivalvular extension represents a critical turning point in the natural history of infective endocarditis and is strongly associated with adverse outcomes. Infection may spread beyond the valve leaflets into adjacent structures, leading to the development of abscesses, pseudoaneurysms, or fistulous communications. These complications reflect a failure of local infection control and frequently occur despite appropriate antimicrobial therapy [14].

The aortic valve is particularly susceptible to perivalvular invasion due to its anatomical proximity to the fibrous skeleton of the heart. Extension of infection into the annulus or surrounding tissue may disrupt structural integrity and facilitate the formation of intracardiac fistulae. Such lesions are associated with rapid clinical deterioration and often necessitate urgent surgical intervention [15].

Persistent bacteremia despite adequate antibiotic treatment may be a clinical clue to underlying perivalvular complications. In addition, the emergence of new conduction abnormalities, such as atrioventricular block, should raise suspicion for extension of infection into the interventricular septum [16]. These findings reflect involvement of the conduction system and may precede overt structural disruption.

Echocardiographic imaging plays a central role in detecting these complications. Transesophageal echocardiography remains the primary diagnostic modality due to its superior spatial resolution and ability to identify abscess cavities and fistulous tracts [17]. Three-dimensional echocardiography may provide additional anatomical detail, particularly in complex lesions. Computed tomography can serve as a complementary tool in selected cases, especially when prosthetic material limits echocardiographic visualization [18].

Once perivalvular extension has developed, the disease process often becomes refractory to medical therapy alone. Surgical intervention is typically required to eradicate infection and restore structural stability. Delayed surgery in this setting may allow further tissue destruction, increasing operative complexity and worsening prognosis.

Hemodynamic Instability

Hemodynamic deterioration remains the most compelling indication for urgent surgical intervention in infective endocarditis. Acute valvular dysfunction resulting from infection-induced structural damage may rapidly compromise cardiac performance. Severe regurgitation, particularly when it develops abruptly, can precipitate pulmonary congestion and circulatory collapse [19].

Acute mitral regurgitation is frequently caused by leaflet perforation or chordal disruption, while acute aortic regurgitation may result from cusp destruction or annular involvement. In both scenarios, the sudden increase in volume overload occurs in a non-adapted ventricle, leading to elevated filling pressures and pulmonary edema. Unlike chronic regurgitant lesions, the absence of compensatory remodeling limits the capacity of the myocardium to maintain forward flow [20].

Prosthetic valve endocarditis may also lead to acute hemodynamic compromise through mechanisms such as prosthetic dehiscence or obstruction. These complications disrupt normal valve function and may result in rapid progression to heart failure. Clinical deterioration can occur even when infection appears microbiologically controlled, reflecting the mechanical consequences of structural damage [21].

Observational studies have consistently identified heart failure as the strongest predictor of mortality in infective endocarditis. Patients presenting with signs of pulmonary edema, hypotension, or low-output state demonstrate markedly worse outcomes when surgery is delayed [22]. Early intervention in the setting of hemodynamic instability has been associated with improved survival, highlighting the importance of prompt recognition.

Waiting for completion of antibiotic therapy in patients with acute valve dysfunction may allow further clinical deterioration and increase operative risk. Surgical timing in these cases should be driven primarily by physiological compromise rather than microbiological considerations.

Neurological Complications and Surgical Timing

Neurological events are among the most common extracardiac complications of infective endocarditis and frequently influence decisions regarding surgical timing. Ischemic stroke occurs in a significant proportion of patients and is typically the result of septic embolization from cardiac vegetations [23]. The presence of neurological injury introduces concerns related to perioperative risk, particularly the possibility of hemorrhagic transformation during cardiopulmonary bypass.

In patients with ischemic stroke, evidence suggests that early surgery may be performed safely in selected cases when neurological deficits are stable and there is no evidence of intracranial hemorrhage. Delaying surgery in such situations may expose patients to additional embolic events or progression of structural cardiac damage [24]. Careful neurological assessment and imaging are essential to guide timing decisions.

In contrast, intracranial hemorrhage represents a major contraindication to immediate surgical intervention. Hemorrhagic lesions are associated with increased risk of expansion during systemic anticoagulation required for cardiopulmonary bypass. Observational studies indicate that postponing surgery for several weeks may reduce perioperative neurological complications in these patients [25].

It is important to recognize that silent cerebral emboli are frequently detected on neuroimaging in patients with infective endocarditis. These lesions often lack clinical manifestation and should not automatically lead to deferral of surgery when other indications are present [26].

Overall, neurological complications necessitate individualized assessment. The type of lesion, stability of neurological status, and urgency of cardiac pathology must be weighed together when determining surgical timing. The relationship between neurological status and surgical timing is summarized in Table 3.

Table 3: Neurological Status and Surgical Timing

Neurological Event	Surgical Strategy	Rationale
Silent cerebral emboli	No delay	Not a contraindication
Stable ischemic stroke	Early surgery possible	Prevent further embolism
Major ischemic stroke	Individualized timing	Risk of hemorrhagic conversion
Intracranial hemorrhage	Delay (≈3–4 weeks)	CPB anticoagulation risk
Septic embolic aneurysm	Evaluate stability	Rupture risk

Abbreviations: *CPB: Cardiopulmonary bypass*

Prosthetic Valve Endocarditis

Prosthetic valve endocarditis represents a distinct and often more aggressive form of infective endocarditis. The presence of foreign material alters host defense mechanisms and facilitates bacterial adherence, leading to a higher likelihood of invasive disease. Compared with native valve infection, prosthetic involvement is associated with increased rates of structural complications and adverse outcomes [27].

A defining feature of prosthetic valve endocarditis is the tendency for infection to extend beyond the prosthetic leaflets into the surrounding annular tissue. This process may result in dehiscence, paravalvular leak, or formation of abscess cavities. Structural instability of the prosthesis can rapidly impair valvular function and contribute to heart failure [28].

In addition to mechanical complications, prosthetic valve endocarditis is frequently associated with persistent infection despite appropriate antimicrobial therapy. The biofilm-forming capacity of microorganisms on prosthetic surfaces may limit antibiotic penetration and promote local extension of disease. This phenomenon underscores the limited effectiveness of medical therapy alone in advanced cases [29].

Delayed surgical intervention in this setting may permit further destruction of the annular support structures and increase operative complexity. Early surgical consideration is therefore often warranted when evidence of prosthetic dysfunction, perivalvular extension, or uncontrolled infection is present [30].

Multidisciplinary Decision-Making

Determining the optimal timing of surgery in infective endocarditis requires integration of clinical, microbiological, anatomical, and neurological data. No single parameter adequately captures disease severity or progression. As a result, decision-making increasingly relies on a coordinated multidisciplinary approach.

Collaboration between cardiologists, cardiac surgeons, infectious disease specialists, and neurologists allows comprehensive assessment of competing risks. Structural damage, embolic potential, neurological status, and hemodynamic stability must be evaluated together rather than in isolation [31]. This integrated perspective is particularly important in complex cases where early surgery may prevent deterioration but carries procedural risk.

The concept of a dedicated endocarditis team has emerged as a strategy to improve outcomes. Observational data suggest that structured collaboration may lead to earlier recognition of surgical indications and more timely intervention [32]. Such teams facilitate rapid interpretation of imaging findings, optimization of antimicrobial therapy, and individualized perioperative planning.

Importantly, reliance on microbiological response alone may be misleading. Clinical improvement in infection parameters does not necessarily reflect stabilization of structural damage or embolic risk. Multidisciplinary evaluation enables surgical timing to be guided by the overall trajectory of disease rather than by isolated laboratory markers.

Clinical Decision Framework

Translating clinical findings into an appropriate surgical timeline requires a structured approach that balances urgency against procedural risk. A practical decision framework should incorporate hemodynamic status, evidence of structural progression, embolic risk, and neurological involvement.

Hemodynamic instability remains the most immediate trigger for surgical intervention. Patients presenting with acute severe valvular dysfunction or signs of heart failure require prompt evaluation for operative management, as further delay may result in irreversible organ injury [33].

Evidence of perivalvular extension represents another decisive factor. The presence of abscess formation, fistulous communication, or new conduction abnormalities indicates ongoing local destruction that is unlikely to resolve with antimicrobial therapy alone [34].

Assessment of embolic risk is also essential. Large or mobile vegetations, particularly on the mitral valve, are associated with a heightened probability of recurrent embolization. Early surgery in such patients may reduce the likelihood of subsequent systemic events [35].

Neurological complications must be carefully integrated into the decision process. While intracranial hemorrhage often necessitates temporary postponement of surgery, ischemic events without hemorrhagic transformation may allow for earlier intervention when cardiac pathology poses an immediate threat [36]. A structured evaluation that integrates these elements can facilitate timely surgical referral and prevent unnecessary delays that may compromise outcomes.

Conclusion

Surgical timing represents one of the most critical determinants of outcome in infective endocarditis. While antimicrobial therapy remains the cornerstone of treatment, progression of structural damage, embolic complications, and hemodynamic deterioration frequently dictate prognosis. Delayed intervention may allow irreversible cardiac injury or systemic complications to develop, particularly in patients with high embolic risk, evolving perivalvular involvement, or acute valvular dysfunction.

Evidence suggests that early surgical consideration is warranted when mechanical instability, persistent local infection, or neurological risk factors threaten clinical stability. Conversely, certain conditions such as intracranial hemorrhage may necessitate temporary postponement to minimize perioperative risk. The challenge lies in balancing these competing considerations through careful assessment of disease trajectory.

A multidisciplinary approach remains essential to guide individualized decision-making. Integration of imaging findings, clinical status, and neurological evaluation enables surgical timing to reflect the overall progression of disease rather than isolated parameters. Infective endocarditis should therefore be regarded as a dynamic condition in which timely surgical intervention can prevent further deterioration. Optimal outcomes depend not only on identifying surgical indications but also on acting before complications become irreversible.

Contribution: All of the authors contributed planning, conduct, and reporting of the work. All authors had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Funding: No financial funding was received for this study.

Conflict of interest: All of the authors have no conflict of interest.

Artificial Intelligence Disclosure: The authors confirm that no artificial intelligence or AI-assisted tools were used for interpreting the referenced article or for generating scientific content. Limited assistance was obtained solely for language editing and grammatical refinement, without any involvement in data interpretation, analysis, or conceptual input.

References

1. Murdoch D.R, Corey G.R, Hoen B, et al. (2009). Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. *Archives of internal medicine*, 169(5):463-473.
2. Habib G, Lancellotti P, Antunes M. J, et al. (2015). 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology

(ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *European heart journal*, 36(44):3075-3128.
3. Kang D.H, Kim Y.J, Kim S.H, et al. (2012). Early surgery versus conventional treatment for infective endocarditis. *The New England journal of medicine*, 366(26):2466-2473.
4. Thuny F, Grisoli D, Collart F, Habib G, Raoult D. (2012). Management of infective endocarditis: challenges and perspectives. *Lancet (London, England),* 379(9819):965-975.
5. Prendergast B.D. (2006). The changing face of infective endocarditis. *Heart (British Cardiac Society)*, 92(7):879-885.
6. Hill E.E, Herijgers P, Claus P, Vanderschueren S, Herregods M.C, Peetermans W.E. (2007). Infective endocarditis: changing epidemiology and predictors of 6-month mortality: a prospective cohort study. *European heart journal*, 28(2):196-203.
7. Anguera I, Miro J. M, Vilacosta I, et al. (2005). Aorto-cavitary fistulous tract formation in infective endocarditis: clinical and echocardiographic features of 76 cases and risk factors for mortality. *European heart journal*, 26(3):288-297.
8. Vilacosta I, Graupner C, San Román J. A, et al. (2002). Risk of embolization after institution of antibiotic therapy for infective endocarditis. *Journal of the American College of Cardiology*, 39(9):1489-1495.
9. Thuny F, Avierinos J.F, Tribouilloy C, et al. (2007). Impact of cerebrovascular complications on mortality and neurologic outcome during infective endocarditis: a prospective multicenter study. *European heart journal*, 28(9):1155-1161.
10. Di Salvo G, Habib G, Pergola V, et al. (2001). Echocardiography predicts embolic events in infective endocarditis. *Journal of the American College of Cardiology*, 37(4):1069-1076.
11. Mohananey D, Mohadjer A, Pettersson G, et al. (2018). Association of Vegetation Size with Embolic Risk in Patients with Infective Endocarditis: A Systematic Review and Meta-analysis. *JAMA internal medicine*, 178(4):502-510.
12. Delgado V, Ajmone Marsan N, de Waha S, et al. (2023). 2023 ESC Guidelines for the management of endocarditis. *European heart journal*, 44(39):3948-4042.
13. Ruttmann E, Willeit J, Ulmer H, et al. (2006). Neurological outcome of septic cardioembolic stroke after infective endocarditis. *Stroke*, 37(8):2094-2099.
14. Ouchi K, Sakuma T, Ojiri H. (2018). Cardiac computed tomography as a viable alternative to echocardiography to detect vegetations and perivalvular complications in patients with infective endocarditis. *Japanese journal of radiology*, 36(7):421-428.
15. Pericas J. M, Llopis J, Cervera C, et al. (2015). Infective endocarditis in patients with an implanted transcatheter aortic valve: Clinical characteristics and outcome of a new entity. *The Journal of infection*, 70(6):565-576.
16. Graupner C, Vilacosta I, SanRomán J, et al. (2002). Periannular extension of infective endocarditis. *Journal of the American College of Cardiology*, 39(7):1204-1211.
17. Habib G, Badano L, Tribouilloy C, et al. (2010). Recommendations for the practice of echocardiography in infective endocarditis. European journal of echocardiography: *the journal of the Working Group on Echocardiography of the European Society of Cardiology*, 11(2):202-219.
18. Feuchtner G. M, Stolzmann P, Dichtl W, et al. (2009). Mult slice computed tomography in infective endocarditis: comparison with transesophageal echocardiography and intraoperative findings. *Journal of the American College of Cardiology*, 53(5):436-444.
19. Tornos P, Iung B, Permanyer-Miralda G, et al. (2005). Infective endocarditis in Europe: lessons from the Euro heart survey. *Heart (British Cardiac Society)*, 91(5):571-575.
20. Tribouilloy C, Rusinaru D, Sorel C, et al. (2010). Clinical characteristics and outcome of infective endocarditis in adults with bicuspid aortic valves: a multicenter observational study. *Heart (British Cardiac Society)*, 96(21):1723-1729.
21. Wang A, Athan E, Pappas P. A, et al. (2007). Contemporary clinical profile and outcome of prosthetic valve endocarditis. *JAMA*, 297(12):1354-1361.
22. Hasbun R, Vikram H. R, Barakat L. A, Buenconsejo J, Quaglia Ello V. J. (2003). Complicated left-sided native valve endocarditis in adults: risk classification for mortality. *JAMA*, 289(15): 1933-1940.
23. Bohbot Y, Habib G, Laroche C, et al. (2022). Characteristics, management, and outcomes of patients with left-sided infective endocarditis complicated by heart failure: a sub study of the ESC-EORP EURO-ENDO (European infective endocarditis) registry. *European journal of heart failure*, 24(7):1253-1265.
24. García-Cabrera E, Fernández-Hidalgo N, Almirante B, et al. (2013). Neurological complications of infective endocarditis: risk factors, outcome, and impact of cardiac surgery: a multicenter observational study. *Circulation*, 127(23):2272-2284.

25. Okita Y, Minakata K, Yasuno S, et al. (2016). Optimal timing of surgery for active infective endocarditis with cerebral complications: a Japanese multicenter study. European journal of cardio-thoracic surgery: *official journal of the European Association for Cardio-thoracic Surgery*, 50(2):374-382.
26. Cooper H. A, Thompson E. C, Laureno R, et al. (2009). Subclinical brain embolization in left-sided infective endocarditis: results from the evaluation by MRI of the brains of patients with left-sided intracardiac solid masses (EMBOLISM) pilot study. *Circulation*, 120(7):585-591.
27. Güray Y, Gücük İpek E, Acar B, et al. (2016). Long-term outcome in patients with prosthetic valve endocarditis: results from a single center in Turkey. Turk Kardiyoloji Dernegi arsivi: *Turk Kardiyoloji Derneginin yayin organidir*, 44(2):105-113.
28. Habib G, Thuny F, Avierinos J. F. (2008). Prosthetic valve endocarditis: current approach and therapeutic options. *Progress in cardiovascular diseases*, 50(4):274-281.
29. Lalani T, Chu V.H, Park L.P, et al. (2013). In-hospital and 1-year mortality in patients undergoing early surgery for prosthetic valve endocarditis. *JAMA internal medicine*, 173(16):1495-1504.
30. Tornos P, Almirante B, Mirabet S, Permanyer G, Pahissa A, Soler-Soler J. (1999). Infective endocarditis due to Staphylococcus aureus: deleterious effect of anticoagulant therapy. *Archives of internal medicine*, 159(5):473-475.
31. Botelho-Nevers E, Thuny F, Casalta J P, et al. (2009). Dramatic reduction in infective endocarditis-related mortality with a management-based approach. *Archives of internal medicine*, 169(14):1290-1298.
32. Chirouze C, Alla F, Fowler V.G, et al. (2015). Impact of early valve surgery on outcome of Staphylococcus aureus prosthetic valve infective endocarditis: analysis in the International Collaboration of Endocarditis-Prospective Cohort Study. *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America*, 60(5):741-749.
33. Athan E, Chu V.H, Tattevin P, et al. (2012). Clinical characteristics and outcome of infective endocarditis involving implantable cardiac devices. *JAMA*, 307(16):1727-1735.
34. Kang N, Wan S, Ng C.S, Underwood M.J. (2009). Periannular extension of infective endocarditis. Annals of thoracic and cardiovascular surgery: *official journal of the Association of Thoracic and Cardiovascular Surgeons of Asia*, 15(2):74-81.
35. Shapiro S, Kupferwasser L.I. (2001). Echocardiography predicts embolic events in infective endocarditis. *Journal of the American College of Cardiology*, 37(4):1077-1079.
36. Barbosa L.Y.C, Feitoza L.M, Scomparin L.M, Conterno L.O, Reis F. (2025). Neurological Complications of Infective Endocarditis. *Revista da Sociedade Brasileira de Medicina Tropical*, 58, e03192025.