

# Early surgery versus antibiotic therapy in patients with infective endocarditis



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## Early Surgery Versus Antibiotic Therapy in Patients with Infective Endocarditis

### Abstract

Infective endocarditis is the infection of the endocardial surface of the heart and heart valves by bacteria or fungi. Choosing the most effective treatment option in patients with IE ensures positive outcome by preventing any possible recurrence and sequelae of the condition. There are currently two approaches to the treatment of infective endocarditis: intravenous antibiotic therapy and surgical valve repair. While intravenous antibiotics are widely regarded as first-line treatment because of its non-invasive approach, it is notable to compare the effectiveness of early surgical treatment to antibiotics in regard to the occurrence of future embolic events and mortality in patients. This article serves to review the pathophysiology of infective endocarditis, and the differences in treatment outcomes.

### Learning objectives

- To discuss the etiology, pathophysiology, and incidence of Infective Endocarditis (IE).
- To explain the available treatment options of IE.
- To discuss factors of increased recurrence and mortality of IE.
- To compare the advantages and disadvantages of treatment options of IE.
- To discuss the research comparing early surgical approach to conventional antibiotic therapy of IE.

## Keywords:

Infective Endocarditis, treatment options, early surgery, intravenous antibiotics, Duke Criteria, thromboembolic events, mortality

## Introduction

Infective endocarditis (IE) is the infection of the endocardial surface of the heart and heart valves. <sup>1</sup> IE can arise from a multitude of bacteria and fungi. <sup>1</sup> *Staphylococcus aureus* is the most common source of infection, and *Streptococcus viridans* is the second most common. <sup>1</sup> Fungi comprise of a small minority of infections seen, and are rare in comparison to bacterial infection. <sup>1</sup> Sources of infection range from intravenous drug use, bacteremia from hospital procedures, implantation of intravenous catheters, and implantable prosthetic devices. <sup>2</sup>

Both native and prosthetic valves can be affected by this condition. Mitral and aortic valves are the most commonly affected native valves due to high pressure of blood flow. <sup>2</sup> Tricuspid valves are commonly affected in intravenous drug users because it is the first intra-cardiac destination of blood flow after venous infiltration. <sup>1</sup> Prosthetic valve endocarditis is less common than native valve endocarditis. <sup>2</sup>

## Pathophysiology

The mechanism of endocardial infection is a stepwise process. There must first be endocardial injury from valvular heart disease, surgery, or

pacemaker wire. <sup>1</sup> Platelet aggregation and fibrin adherence occurs as the body tries to fix that injury. <sup>2</sup> This sterile platelet-fibrin nidus serves as a prime area for bacteria to adhere because this inflammation is not as smooth as regular tissue. <sup>3</sup> Microorganisms circulating in the blood, either from a distant source of focal infection or bacteremia from a mucosal or skin source, adhere to the nidus. <sup>3</sup> The microorganisms proliferate in the thrombus, thus forming the classic vegetation on the endocardium and heart valve. <sup>3</sup>

### Epidemiology

The incidence of IE is between 2 and 10 episodes per 100, 000 person-years in most population-based studies. <sup>1</sup> About 15, 000 new cases are diagnosed every year in the United States. <sup>2</sup> This accounts for 1 in 1000 hospital admissions. <sup>2</sup> IE is more common amongst men compared to women, and seen more in elderly patients. <sup>4</sup> In the pre-antibiotic era, the mean age of patients effected was around 30 years. <sup>4</sup> However, the post-antibiotic era has led to a shift in the mean age affected to 60 years. There has been some discussion that the incidence of infective endocarditis is declining because of advanced treatment of rheumatic heart disease. <sup>1</sup> Rheumatic heart disease is a condition that can lead to the formation of IE. <sup>2</sup>

Epidemiology of the disease can aid in its recognition and prompt treatment. IE is more common in men than in women, and found more in patients greater than 60 years. <sup>1</sup> There are conditions that predispose patients to a greater risk of IE such as rheumatic heart disease with mitral stenosis. <sup>2</sup>

Heart conditions such as rheumatic heart disease and congenital heart disease predispose a patient to IE due to turbulent blood flow.<sup>3</sup> About 75% of patients with infective endocarditis have an underlying structural heart disease.<sup>1</sup>

Valvular defects such as mitral regurgitation, aortic stenosis, and aortic regurgitation can predispose patients to IE.<sup>5</sup> Previous endocarditis increases the likelihood of a recurrent case.<sup>4</sup> Prosthetic valves increase the risk of infective endocarditis.<sup>1</sup> Mechanical valves are associated with hemolysis and are thrombogenic, requiring lifelong anticoagulation.<sup>6</sup> The high propensity for clot formation in mechanical valves serves as a nidus for bacterial or fungal aggregation.<sup>6</sup> The highest risk of IE is the highest within the first year after implantation of the valve.<sup>6</sup> Intravenous drug use, and implantation of central venous catheters increase risk of IE due to bacterial infestation into blood.<sup>4</sup>

## Presentation

Typical patients are above the age of 60 who presents with fever, fatigue, and new onset heart murmur.<sup>4</sup> They can present with cardiac complications, neurologic complications, septic emboli, infection, and/or systemic immune reaction.<sup>3</sup> Cardiac complications are seen in up to 50% of patients, and include valvular insufficiency and heart failure.<sup>1</sup> Neurologic complications are seen in up to 40% of patients, and include embolic stroke, intracerebral

hemorrhage, or brain abscess.<sup>5</sup> Septic emboli are seen in up to 25% of patients, and include infarct of kidneys, spleen, and other organs.<sup>5</sup>

There are many physical exam manifestations in patients with IE. The most common manifestation is a cardiac murmur, and is seen in about 85% of IE patients.<sup>3</sup> Other findings include splinter hemorrhages, which are hemorrhagic lesions on the nail beds, and Janeway Lesions, which are non-tender, erythematous macules on palms and soles. Additionally, Osler Nodes, which are tender, subcutaneous violaceous nodules mostly on pads of fingers and toes and Roth Spots, which are exudative, edematous hemorrhagic lesions of retina with pale centers are classic findings in an endocarditis patient.

## Diagnosis

Diagnosis of infective endocarditis involves the incorporation of the Duke Criteria.<sup>3</sup> The Duke Criteria uses information from echocardiography, microbiology, history, and physical exam to compile points that would confirm diagnosis of IE. Two major criteria or one major and three minor criteria confirm definitive endocarditis.<sup>5</sup>

Major criteria are positive blood cultures from 2 separate blood cultures that contain typical organisms like *Streptococci viridans* or *Staphylococcus aureus*, and evidence of endocardial involvement by positive echocardiography for vegetation or abscess.<sup>4</sup> Minor criteria are predisposition with IVDA or heart condition, fever, vascular phenomena,

immunologic phenomena, or positive blood cultures that do not meet the major criteria.<sup>3</sup>

### Current Treatment and Management

There are currently two treatment modalities for IE: IV antibiotics and surgery.<sup>4</sup> The treatment of choice for patients with IE is intravenous antibiotics.<sup>2</sup> This consists of a combination of antibiotics infused in an inpatient setting. Antibiotic choice differs based on the causative organism of infection. The treatment for streptococcus and enterococcus is IV Penicillin G, Ceftriaxone +/- Gentamicin or Vancomycin.<sup>1</sup> Treatment for Staphylococcus is usually Gentamycin, rifampin, and vancomycin.<sup>5</sup> Treatment for a fungal infection is IV amphotericin B.<sup>6</sup>

Surgery is also a treatment modality for patients diagnosed with IE.<sup>7</sup> Surgical treatment involves repair or replacement of the damaged heart valve.<sup>7</sup> Current indications for surgical treatment include antibiotic failure, abscess formation, and fungal infection.<sup>7</sup> Valve replacement eventually is needed in many patients due to progressive valve damage, or in those patients in which recurrence of the condition occurs.<sup>7</sup>

### Adverse Effect Profile of Surgery and Antibiotics

Adverse effects are important to consider when choosing the best treatment modality for infective endocarditis. Surgery adverse effects and complications include the risk of bleeding, infection, blood clots, pneumonia,

and death. These risks are important to consider in surgery of any type. Moreover, weighing the risks versus the benefits can immensely affect the treatment choice.

Adverse effects of antibiotics include anaphylaxis, Steven Johnson syndrome, neurotoxicity, nephrotoxicity, and superinfection. A patient who is refractory to antibiotic treatment, develops resistance, or is allergic to the first-line antibiotics may be considered good candidates for surgery.

### Treatment Considerations

Successful treatment of any condition accounts for sequelae, recurrence, and mortality. A decrease in these three factors in addition to elimination of the initial disease process ensures high quality of care. Thus, treatment of infective endocarditis should first and foremost aim to treat the primary infection. It is, however, important to treat infection to also prevent sequelae and mortality. This begins with identification of the complications and deciding on a treatment plan that has the highest likelihood to prevent them.

Perhaps the most important acute sequela of IE is a thromboembolic event in which valvular vegetation seeds off and occludes vasculature to vital organs. Two major examples of such an event is obstruction of carotid artery outflow, leading to stroke, and obstruction of pulmonary artery outflow, leading to pulmonary embolism. In contrast to acute complications, the most common chronic issue seen in patients with IE, as stated earlier, is congestive heart failure.



While intravenous antibiotics is considered first-line treatment as it is the least invasive option,

surgery has been a treatment development in the last 25 years.<sup>9</sup> This is done by means of valve replacement. Some research states that about 60% of patients will have to be operated on at some time in their life.<sup>8</sup> This statistic arises from the idea that many patients with IE have underlying heart disease and others have direct acute consequences of IE such as those listed previously.

There are few studies that focus on the effectiveness of surgery in preventing sequelae and mortality, particularly in comparison to antibiotics. This CME focuses on pivotal studies that address these issues. These studies may help a provider make the decision on a treatment plan based on the patient's medical history, and may spark future research in formulating criteria to make the best treatment choice, whether that be intravenous antibiotics or early surgical treatment.

#### Treatment Outcomes in Native Valve Endocarditis

This prospective, randomized controlled trial was conducted to determine whether early surgery would decrease the rate of embolic events, as compared to conventional treatment of intravenous antibiotics. Early surgery defined by this study was within 48 hours of randomization, and bypassing the AHA recommended guidelines of beginning with antibiotic therapy.<sup>2</sup> The <https://assignbuster.com/early-surgery-versus-antibiotic-therapy-in-patients-with-infective-endocarditis/>

authors targeted patients specifically with severe left-sided, native-valve infective endocarditis.<sup>2</sup> Patients with large heart valve vegetations were randomly assigned to either early surgery or conventional treatment. The end points of focus was a composite of in-hospital death and embolic events that occurred within 6 weeks and 6 months after randomization.<sup>2</sup> The authors found that early surgery is protective in that a patient has a decreased likelihood of an embolic event or mortality in the hospital after procedure or at 6 weeks after early surgery as compared to the conventional treatment of antibiotics.<sup>2</sup> They also found that there was no significant difference between the two groups in mortality at 6 months after randomization, but a significant decrease in embolic events and recurrence of infection in the early surgery group in comparison to the conventional treatment group.

The drawbacks to the study were that patients with only left sided valves, but no right sided valves were included. Right sided valves are important to incorporate because of the prevalence of right sided infection seen in intravenous drug users, and the complication of septic pulmonary embolism.

<sup>2</sup> Albeit the good method of randomization and study design, the sample size was under 100 patients and prosthetic valve patients were excluded from the study. This study is targeted toward providers in cardiology and internal medicine who are also curious about the treatment approach of endocarditis. By finding that the rate of in-hospital mortality and embolic events are significantly decreased with early surgery rather than antibiotics, this can open up future studies that observe long term effects and mortality, and

perhaps optimize treatment approach to reduce recurrence of endocarditis in patients.

A similar study with over 300 participants with left-sided IE found that there was a benefit in early surgery, as it reduced the risk of in-hospital and 12 month mortality compared to medical treatment.<sup>14</sup> The main indications for surgery in this study were congestive heart failure and valvular disorder. This study was not a randomized controlled trial, and instead focused on a cohort of over 1000 patients over the course of 20 years. Thus, confounding variables may skew the results. The main idea was that a significant decrease in mortality was seen mainly in those patients that had pre-existing moderate to severe congestive heart failure.<sup>14</sup> The idea behind this is that valvular replacement procures a higher magnitude of hemodynamic benefit compared to patients with no congestive heart failure. This study is beneficial in that it can help providers make the distinction of need for surgery based on their severity of presenting status of congestive heart failure.

#### Treatment Outcomes in prosthetic valve endocarditis

A prospective, observational cohort study aimed to determine the in-hospital and 1-year mortality in patients with prosthetic valve endocarditis who undergo valve replacement during hospitalization compared with patients who receive medical therapy alone.<sup>3</sup> The authors included patients hospitalized with definite right or left sided prosthetic valve endocarditis, and evaluated the effect of treatment assignment on mortality over the span of six years.<sup>3</sup> In this study, it was found that there was not a statistically  
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significant difference in 1-year mortality in patients with prosthetic valve endocarditis as opposed to receiving solely medical therapy.<sup>3</sup>

While this study initially found that early surgery was associated with a mortality benefit, this benefit was neutralized when controlling for survivor bias in the cohort. Those groups who were indicated for surgery, such as patients with valve regurgitation and abscessed patients, were found to have a lower one-year mortality rate.<sup>3</sup> This study was strong in that it is the largest study in medical literature that focuses specifically on prosthetic valve endocarditis.<sup>3</sup> Additionally, the data spans internationally from centers whose expertise include infective endocarditis. This study may not be externally valid because most of the institutions where data was obtained from contain voluntary participation, which implies that referral bias may influence outcome. Additionally, while patients were prescribed early surgery in the study, the time in between diagnosis of prosthetic valve endocarditis and new prosthetic valve implantation was not mentioned. This may have an effect on mortality rate data. This study targets providers looking for corroborating evidence that there may not be a significant difference in the treatment preferences for patients with endocarditis who do not have a high indication for surgery in the first place.

## Conclusion

Infective endocarditis (IE) is the infection of the endocardial surface of the heart and heart valves.<sup>11</sup> The prevalence of IE is on the decline in the United States, but the rate of recurrence, sequelae, and mortality is an important

topic to address for patient care.<sup>8</sup> Considering treatment choice may aid in reducing the rate of these factors.<sup>6</sup> Early surgery may have a benefit in preventing a future embolic event and decreasing short and long-term mortality in comparison to the conventional route of early antibiotic therapy.<sup>2, 3, 14</sup> Invasive, early surgery in the form of valve replacement can ensure vegetation is adequately removed, and can provide a significantly better rate of mortality, especially in patients with heart failure.<sup>14</sup> However, the decision for early surgery may be heavily contingent on the patient having congestive heart failure and left-sided infective endocarditis.<sup>3, 14</sup> While conclusions can be made based on the specific studies in this CME, future studies would be needed to strengthen evidence showing the benefit of early surgery in right sided endocarditis.

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