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Surgical Management of Mitral Valve Endocarditis

Fabian Andres Giraldo Vallejo

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Abstract

Before the antibiotic era and cardiac surgery, infective endocarditis (IE) was a predominantly fatal disease. In-hospital mortality persists relatively high despite development in medical and surgical treatment. Adequate timing and surgical management of the infected valve help prevent substantially early and late mortality. The surgical approach of mitral valve endocarditis should be based on extension of the disease and annular involvement. When the valve and annulus are severely affected, the best option is to perform a complete excision and mitral valve replacement (MVR). Only if the disease is limited to the valvular tissue, mitral valve repair is the preferred surgical option.

Keywords: infective endocarditis, epidemiology of infective endocarditis, mitral valve surgery, mitral valve repair, periannular abscess

1. Introduction

The term *infective endocarditis* (IE) refers to infection of the endocardial surface of the heart. Infection may affect heart valves mainly but may occur within a septal defect, in chordae tendinae, or in the mural endocardium. Shunt infections (e.g., arteriovenous shunts, arterioarterial shunts (patent ductus arteriosus)) or coarctation of the aorta is similar in presentation to IE. The main site of cardiac involvement is on the line of closure of a valvar surface. Most affected sites are the atrial side of the atrioventricular valves or on the ventricular surface of the semilunar valves [1].

Perhaps the most convincing hypothesis for the pathogenesis of IE has been given to Rodbar in which high velocity flows from a high-pressure source form in an orifice and enter a low-pressure sink. Bacteria are deposited through *Venturi currents* beyond the orifice to form vena contracta creating mechanical erosion and deposition of platelets and thrombin [2].

Diagnostic criteria for IE were published in 1982 by von Reyn et al. (the Beth Israel Criteria), but these criteria did not include echocardiographic findings in the case definitions [3]. Including the important role of echocardiography in the evaluation of suspected IE, new case definitions and diagnostic criteria were proposed in 1994 [4], modified in 2000 and broadly used since then [5]. The usefulness of echocardiography in the diagnosis of IE is clearly known [6]; transesophageal imaging has superior sensitivity and specificity, is cost-effective, and should be done when transthoracic approach is negative and the patient has a high clinical suspicion of IE.

Even though the infected aortic valve is difficult to repair, well-known repair techniques can be applied to patients with mitral valve endocarditis. Advantages of mitral valve repair compared with replacement are well established for noninfectious mitral valve disease and include low perioperative mortality, preserved left ventricular function, no need for long-term anticoagulation, less long-term thromboembolic complications, lower risk of IE, freedom from reoperation, and improved long-term survival [7].

2. Clinical features and diagnostic criteria

Investigators at Duke University modified the terms introduced by Jones (rheumatic fever); these criteria include major and minor signs and symptoms, echocardiographic findings, iatrogenic and nosocomial factors (indwelling catheters), and history of IV drug abuse (**Table 1**) [5]. The most common clinical manifestation of IE is fever, which can be present in 95–100% of patients. Fever may present as low grade or spiking following peak of bacteremia. It is important to draw two sets of blood cultures from different sites in any patient at risk of having IE who presents with fever of unknown origin for more than 48 h. Once blood cultures have been obtained, antibiotics should be started until proper identification of causative organism [8]. When IE is confirmed by echocardiography, surgery, or autopsy, positive blood cultures are obtained in 95% of cases when two blood specimens are obtained and are positive in 98% of cases with four blood specimens [9]. However, when dealing with prosthesis valve endocarditis (PVE), a negative-culture endocarditis can rise to about 10% of cases on most surgical series [10, 11]. The diagnosis of IE should be investigated in any patient with sepsis of unknown origin or fever associated with risk factors. Sepsis can present in a variety of forms and can range from malaise to shock depending on the virulence of the pathogen and the host immune response [12, 13]. Stroke or systemic embolism can also be present as a complication of IE. Whenever a patient presents with persistent or unexplained bacteremia, the diagnosis of IE should be ruled out. *S. aureus* bacteremia is associated with IE in 25–30% of cases, and all patients should undergo echocardiography [14, 15]. Risk factors for developing IE include previous IE, a prosthetic valve or cardiac device and valvular or congenital heart disease, indwelling intravenous lines, intravenous drug use, immunosuppression, and a recent dental or surgical procedure. Popular known signs like Osler's nodes, Janeway lesions, and Roth spots are rare; their absence does not rule out infective endocarditis. Heart failure, stroke, or metastatic infection (osteomyelitis, peripheral abscess) are much more common. Routine laboratory tests are usually nonspecific. Admission electrocardiogram is useful since new disturbances may suggest paravalvular or myocardial extension of infection [16].

Definite infective endocarditis

Pathologic criteria

- Microorganisms demonstrated by culture or histologic examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen
- Pathologic lesions; vegetation or intracardiac abscess confirmed by histologic examination showing active endocarditis

Clinical criteria

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

Possible infective endocarditis

- One major criterion and one minor criterion
- Three minor criteria

Rejected

- Firm alternate diagnosis explaining evidence of IE
- Resolution of IE syndrome with antibiotic therapy for ≤ 4 days
- No pathologic evidence of IE at surgery or autopsy, with antibiotic therapy for ≤ 4 days
- Does not meet criteria for possible IE, as above

Major criteria

Blood culture positive for IE

- Typical microorganisms consistent with IE from two separate blood cultures: viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*
- Community-acquired enterococci, in the absence of a primary focus
- Microorganisms consistent with IE from persistently positive blood cultures, defined as follows:
 - At least two positive cultures of blood samples drawn >12 h apart
 - All of three or a majority of $\geq$ four separate cultures of blood (with the first and last samples drawn at least 1 h apart)
 - Single positive blood culture for *Coxiella burnetii* or antiphase I IgG antibody titer $>1:800$

Evidence of endocardial involvement

- Echocardiogram positive for IE (TEE recommended in patients with prosthetic valves, rated at least “possible IE” by clinical criteria or complicated IE [paravalvular abscess]; TTE as first test in other patients), defined as follows:
 - Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation
 - Abscess
 - New partial dehiscence of prosthetic valve
 - New valvular regurgitation (worsening or changing of preexisting murmur not sufficient)

Minor criteria

- Predisposition, predisposing heart condition or injection drug use
- Fever, temperature $> 38^{\circ}\text{C}$ (100.4°F)
- Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway lesions
- Immunologic phenomena: glomerulonephritis, Osler’s nodes, Roth’s spots, and rheumatoid factor
- Microbiologic evidence: positive blood culture but does not meet a major criterion as noted above* or serologic evidence of active infection with organism consistent with IE
- Echocardiographic minor criteria eliminated

HACEK, *Haemophilus* spp., *Aggregatibacter* spp., *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* spp.; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography
 Modified from Li et al. [5].

Table 1. Definition of infective endocarditis (IE) according to modified Duke criteria.

Diagnosis of IE includes the sum of clinical findings, microbiological analysis, and imaging results. A definite diagnosis includes two major modified Duke criteria, one major plus three minor and five minor criteria [5]. Alternatively the diagnosis can be made by specimen culture or histology (obtained by surgery or autopsy) of the vegetation or abscess. The physician must note that Duke criteria were devised to help in the diagnosis but never to replace the clinical judgment [17].

Infection of the mitral valve and its supporting structures is less frequent than aortic valve endocarditis but may be more indolent in its course. When *S. aureus* is the infecting organism, the mitral valve is more frequently involved ($\pm 40\%$ of cases) followed by the aortic valve in 36% of cases [18]. Echocardiography plays a major role in diagnosis and detection of complications. A major criterion includes the presence of valvular vegetation or abscess or new dehiscence of a prosthetic valve [19]. Besides diagnostic, echocardiography also provides information on the hemodynamic status of the valve lesion and left and right ventricular function. In native valve endocarditis (NVE), transthoracic echocardiography (TTE) has a sensitivity of 75% and specificity of $>90\%$ for detection of a vegetation. Transesophageal echocardiography (TEE) has a sensitivity $>90\%$ and should be done in a patient with a negative or equivocal TTE and high clinical likelihood of infective endocarditis [19]. As for abscess, leaflet perforation or pseudoaneurysm TEE offers better detection than TTE [20, 21]. In patients with prosthetic valves, the sensitivity of TTE is lower (36–69%), and TEE is more accurate in detecting complications and cardiac device infections [22, 23].

3. Therapy

The management of patients with IE necessitates a multidisciplinary approach where cardiologists, cardiac surgeons, and infectious disease specialists are involved. There are no clinical randomized trials that guide the management decisions nor a level A evidence in international guides [8, 24].

3.1. Antibiotics

Antibiotics should be started once blood cultures have been acquired; nevertheless if the patient is stable, the physician could wait until final report is available [25]. Empirical antibiotic regimens for the native valve endocarditis and prosthetic valve endocarditis are outlined on definite guidelines by the British Society for Antimicrobial Chemotherapy (**Table 2**) [25]. Antibiotics can be modified according to culture results, local resistance patterns, virulence, and the presence or absence of prosthetic material. Because penetration of antibiotics to vegetations is difficult, prolonged parenteral antibiotic administration is advisable. Treatment for at least 4–6 weeks is usually necessary and longer for some cases (e.g., Q fever endocarditis).

3.2. Surgery

About 40–50% of patients with IE undergo surgical therapy [26, 27]. Goals of surgery are removal of infected tissue and drainage of abscess, restoration of ventriculoarterial or atrio-ventricular continuity, and reversion to hemodynamic stability. In children, this process may

	Empirical antibiotic regimen and dose	Comment
Native valve endocarditis—indolent presentation	Amoxicillin (2 g, every 4 h, intravenously) + gentamicin* (optional; 1 mg/kg of actual bodyweight)	Better activity than benzylpenicillin against enterococci and many HACEK bacteria; the use of gentamicin before availability of culture results is controversial
Native valve endocarditis—severe sepsis (without risk factors for multiresistant enteric Gram-negative bacilli, <i>Pseudomonas</i>)	Vancomycin* (dose as per local guidelines) + gentamicin* (1 mg/kg of ideal bodyweight, every 12 h, intravenously)	Activity against staphylococci (including meticillin-resistant <i>Staphylococcus aureus</i>)
Native valve endocarditis—severe sepsis (with risk factors for multiresistant enteric Gram-negative bacilli, <i>Pseudomonas</i>)	Vancomycin* (dose as per local guidelines) + meropenem (2 g, every 8 h, intravenously)	
Prosthetic valve endocarditis—pending blood cultures or with negative blood cultures	Vancomycin* (1 g, every 12 h, intravenously) + gentamicin* (1 mg/kg, every 12 h, intravenously) + rifampicin (300–600 mg, every 12 h, orally or intravenously)	

Adapted from Gould et al. [25].

All antibiotic doses are adjusted according to renal function. HACEK=*Haemophilus* spp., *Aggregatibacter actinomycetem-comitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kinga*.

*Regular measurement of serum concentrations needed to monitor and adjust dosing.

Table 2. Empirical treatment for different clinical scenarios in patients with suspected infective endocarditis.

require repairing of the underlying malformation. Valve repair and replacement are options for reconstruction, and there is no evidence that favors a bioprosthetic valve over a mechanical valve. *Heart failure* caused by valvular obstruction or regurgitation is the most common indication for surgery. A dismal prognosis is ensued when refractory pulmonary edema or cardiogenic shock is present and no emergent surgery is done [28, 29].

There is limited evidence to guide clinical practice when the patient has well-tolerated severe valve regurgitation and postpone surgery until stabilization with antibiotics. *Complex or uncontrolled infection* is the second indication for surgery. The complications include abscess, pseudoaneurysm, fistula, or atrioventricular block. A pseudoaneurysm is a perivalvular cavity that communicates with the cardiac chambers (evidenced by Doppler color), whereas an abscess is a pus-filled perivalvular cavity that does not communicate [19]. If perivalvular infection progresses, a fistula can be created (usually aorto-cavitary) which can have a mortality as high as 41% even with surgery [30]. *Prevention of embolism* is the third indication for surgery. This complication can affect 25–50% of patients [31]. Stroke is the most common presentation, but embolism resulting in end-organ infarction (kidney, spleen, coronaries, mesentery, and limbs) can also be present. Most emboli occur in the first 2 weeks after diagnosis with risk decreasing rapidly after antibiotics are instituted [32, 33]. Embolism is more likely when the vegetation is large (>10 mm), highly mobile, and located in the mitral valve [34]. *Persistent or relapsing infection* and infection caused by antibiotic-resistant microorganisms (e.g., *S. aureus*, *S. lugdunensis*, *Pseudomonas*, fungi) are also indications for surgery [27].

Surgery for IE is done through partial or full median sternotomy. Suppurative pericarditis suggests a previous perforation at the aortic or mitral ring or ring abscess [35, 36]. It is recommended to use bicaval cannulation to facilitate the procedure in the presence of burrowing abscess, acquired septal perforation, unexpected right-sided valve involvement, or complex aortic root reconstruction. Intraoperative TEE plays a major role in diagnosis and treatment guidance. When left-sided IE is present, minimal manipulation of the heart is important to avoid migration of embolic material. Ample excision of infected tissue is performed with drainage of abscess and closure of defects [37]. When mitral endocarditis is present, aortic valve involvement should be considered. Although absence of echocardiographic anomalies in the aortic area argue against the presence of vegetations and inspection of the aortic valve is not necessary. Reconstruction on mitral valve area can be accomplished when the vegetation is healed or small and the tensor apparatus is mostly uncompromised. Usual sites of native valve endocarditis are drop lesion of anterior leaflet or leaflet vegetation and ring abscess of posterior portion (**Figure 1**). Small perforations may be closed using autologous pericardium or bovine pericardial patch, or otherwise the defect may be closed using continuous suture (**Figure 2**). Reconstruction of the mitral valve represents a challenge if major involvement of the valves is present. Most of the times, a replacement is considered; nevertheless, the risk for PVE is greater especially in ongoing positive blood cultures. If commissural areas are compromised by the infection, a sliding annuloplasty can be performed. Partial leaflet resection, pericardial patch replacement of mid-leaflet areas, or both may be used [37]. The remaining orifice size after reconstruction must be large enough (25 mm in an adult, z-score -2 or greater in children) to prevent mitral stenosis [37]. Suture annuloplasty is preferable over prosthetic ring in active IE, but a biodegradable annuloplasty ring has been suggested by some authors [38]. In the absence of active IE (e.g., negative blood cultures, no inflammation), classical reconstruction techniques may be used for the mitral valve. Quadrangular resection of a portion of the posterior leaflet (**Figure 3**) or triangular resection of a portion of the anterior leaflet may be done, followed by the insertion

Figure 1. Drop lesion of anterior leaflet and leaflet vegetation and ring abscess of posterior leaflet.

Figure 2. Pericardial patch used to close a drop lesion of the anterior leaflet.

Figure 3. Limited quadrangular resection and sliding plasty of posterior leaflet.

of a partial or complete annular ring. When resecting the mitral valve, the posteroinferior zone of the mitral annulus should be inspected because myocardial ring abscess usually occurs in this location [39, 40]. When left atrioventricular discontinuity is present in mitral valve IE, a small variation of the usual valve replacement can be used. After thorough debridement of the affected tissue in the mitral ring, interrupted horizontal mattress sutures are anchored with felt or autologous pericardium pledgets to the ventricular aspect of the mitral annulus, brought up through the left atrial aspect and then through the prosthetic sewing ring. Deep bites are performed [37]. When extensive ring abscess is present (**Figure 4**), a different approach is done. The atrioventricular discontinuity is reconstructed using an autologous or bovine pericardial patch. The ventricular aspect is anchored to the myocardium and endocardium using deep bites of continuous 3-0 or 4-0 polypropylene suture. The superior aspect of this patch is anchored to the left atrial side with a continuous suture (**Figure 5**). The prosthesis is anchored to the ventricular aspect of the suture line using interrupted horizontal mattress sutures supported with felt pledgets (**Figure 6**) [37]. Using antibiotic, antiseptic solutions (e.g., povidone-iodine), or antifungal agents to impregnate the prosthesis and the affected area has been described to help in the management of this entity [41–43]. Mitral valve repair for IE continues to be challenging and much less commonly performed than valve replacement [44]. Repairing tissues that may be infected in the acute stages and the durability of repairing inflamed tissues are the main concerns influencing the decision [45–47]. Several studies have reported excellent results for mitral valve repair in IE [48–51].

Figure 4. Infective endocarditis with ring abscess compromising the posterior leaflet of mitral valve.

Figure 5. The defect is covered by a pericardial patch anchored within the left ventricle and extending up across the base of the posterior leaflet. Stitches then are placed to the left atrial wall.

Figure 6. Prosthesis is placed in position. The posterior suture line is on the patch in this case. Eventually the prosthesis may be seated below the patch on ventricular wall.

4. Results

Hospital mortality for valve operations in patients with IE varies widely (4–30%) [52–57]. This variation can be due to several factors, especially the difference in risk between the acute phase of IE and the healed stage. A study from Richardson reported a mortality of 14% in surgically treated patients versus 44% in those medically treated. Operative mortality was affected by urgency of operation. Mortality for elective operations (next convenient day), was 5%, for urgent operations (next day), 16% and for emergent operations in patients with cardiogenic shock (immediately), 33% [58].

Freedom from reoperation is higher when the mitral valve is involved (compared with the aortic valve) probably for less annular involvement. In a series from Brigham and Women's Hospital (Boston) reporting freedom from reoperation for mitral valve IE, the results found 92 and 62% at 5 and 10 years for acute endocarditis and 94% and 84% for healed endocarditis ($p = 0.7$), respectively [59]. A serious complication after valve replacement for IE is a new or worsening neurologic deficit. Friable vegetation may dislodge and cause CNS deficits. Moreover, an existing CNS deficit is aggravated by operation. A study from university of Illinois found evidence of cerebral septic emboli in 42% of patients who underwent valve replacement for IE. Complications included postoperative strokes in 6%, brain abscesses in 2%, and seizures in 1% [60].

5. Indications for operation

Indications for operation are based in the hemodynamic state of the valvar lesion or defect. When active NVE is present, a lack of consensus exists about some of the specific indications for surgery [61]. General indications for operation, however, exist from both the American and European societies (**Table 3**) [8, 24]. As for timing of surgery, specific recommendations are outlined in **Table 4** [26]. However it is important to remember that no randomized controlled

Congestive heart failure*

- Congestive heart failure caused by severe aortic or mitral regurgitation or, more rarely, by valve obstruction caused by vegetations
- Severe acute aortic or mitral regurgitation with echocardiographic signs of elevated left ventricular end-diastolic pressure or significant pulmonary hypertension
- Congestive heart failure as a result of prosthetic dehiscence or obstruction

Periannular extension

- Most patients with abscess formation or fistulous tract formation

Systemic embolism[†]

- Recurrent emboli despite appropriate antibiotic therapy
- Large vegetations (10 mm) after one or more clinical or silent embolic events after initiation of antibiotic therapy
- Large vegetations and other predictors of a complicated course
- Very large vegetations (15 mm) without embolic complications, especially if valve-sparing surgery is likely (remains controversial)

Cerebrovascular complications[‡]

- Silent neurological complication or transient ischemic attack and other surgical indications
- Ischemic stroke and other surgical indications, provided that cerebral hemorrhage has been excluded and neurological complications are not severe (e.g., coma)

Persistent sepsis

- Fever or positive blood cultures persisting for >5 to 7 days despite an appropriate antibiotic regimen, assuming that vegetations or other lesions requiring surgery persist and that extracardiac sources of sepsis have been excluded
- Relapsing IE, especially when caused by organisms other than sensitive streptococci or in patients with prosthetic valves

Difficult organisms

- *S. aureus* IE involving a prosthetic valve and most cases involving a left-sided native valve
- IE caused by other aggressive organisms (*Brucella*, *Staphylococcus lugdunensis*)

- IE caused by multiresistant organisms (e.g., methicillin-resistant *S. aureus* or vancomycin-resistant enterococci) and rare infections caused by Gram-negative bacteria
- *Pseudomonas aeruginosa* IE
- Fungal IE
- Q fever IE and other relative indications for intervention

Prosthetic valve endocarditis

- Virtually all cases of early prosthetic valve endocarditis
- Virtually all cases of prosthetic valve endocarditis caused by *S. aureus*
- Late prosthetic valve endocarditis with heart failure caused by prosthetic dehiscence or obstruction or other indications for surgery

*Surgery should be performed immediately, irrespective of antibiotic therapy, in patients with persistent pulmonary edema or cardiogenic shock. If congestive heart failure disappears with medical therapy and there are no other surgical indications, intervention can be postponed to allow a period of days or weeks of antibiotic treatment under careful clinical and echocardiographic observation. In patients with well-tolerated severe valvular regurgitation or prosthetic dehiscence and no other reasons for surgery, conservative therapy under careful clinical and echocardiographic observation is recommended with consideration of deferred surgery after resolution of the infection, depending upon tolerance of the valve lesion.

†In all cases, surgery for the prevention of embolism must be performed very early since embolic risk is highest during the first days of therapy.

‡Surgery is contraindicated for at least 1 month after intracranial hemorrhage unless neurosurgical or endovascular intervention can be performed to reduce bleeding risk.

Adapted from ACC/AHA 2014 Guidelines [8].

Table 3. Indications for surgery for infective endocarditis.

Emergency surgery (within 24 h)

- Native (aortic or mitral) or prosthetic valve endocarditis and severe congestive heart failure or cardiogenic shock caused by:
 - Acute valvular regurgitation
 - Severe prosthetic dysfunction (dehiscence or obstruction)
 - Fistula into a cardiac chamber or the pericardial space

Urgent surgery (within days)

- Native valve endocarditis with persisting congestive heart failure, signs of poor hemodynamic tolerance, or abscess
- Prosthetic valve endocarditis with persisting congestive heart failure, signs of poor hemodynamic tolerance, or abscess
- Prosthetic valve endocarditis caused by staphylococci or Gram-negative organisms
- Large vegetation (10 mm) with an embolic event
- Large vegetation (10 mm) with other predictors of a complicated course
- Very large vegetation (15 mm), especially if conservative surgery is available
- Large abscess and/or periannular involvement with uncontrolled infection

Early elective surgery (during the in-hospital stay)

- Severe aortic or mitral regurgitation with congestive heart failure and good response to medical therapy
- Prosthetic valve endocarditis with valvular dehiscence or congestive heart failure and good response to medical therapy
- Presence of abscess or periannular extension
- Persisting infection when extracardiac focus has been excluded
- Fungal or other infections resistant to medical cure

Adapted from Prendergast et al. [26].

Table 4. Timing of surgery.

trials are available to guide current practice. Among the indications for surgery in IE, operation for acute heart failure provides the greatest survival benefit [62, 63].

Infective endocarditis is a serious condition associated with significant morbidity and mortality. Adequate management requires intervention of multiple specialists. Correct and timed diagnosis and antibiotics are necessary, but an important percentage of patients still require surgery. Surgical mortality is high, but long-term results continue to improve with increased number of patient undergoing valve conserving surgery.

Author details

Fabian Andres Giraldo Vallejo

Address all correspondence to: fabiangiraldomd@gmail.com

Instituto del Corazón de Bucaramanga, Bucaramanga, Colombia

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