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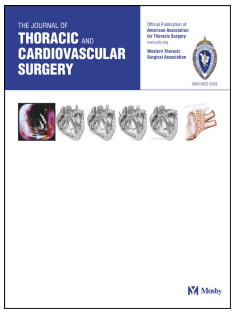

2016 American Association for Thoracic Surgery (AATS) Consensus Guidelines: Surgical Treatment of Infective Endocarditis

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2016 American Association for Thoracic Surgery (AATS) Consensus Guidelines: Surgical Treatment of Infective Endocarditis

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See Online Data Supplement 1

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PREAMBLE

Our mission was to develop evidence-based consensus guidelines for surgical treatment of infective endocarditis (IE).[1] The writing committee included 4 cardiac surgeons, 1 cardiologist, 2 infectious disease specialists, and Dr. Eugene H. Blackstone. An additional group of experts, including 4 cardiac surgeons, 1 anesthesiologist, 1 cardiologist, 2 imaging experts, 3 infectious disease specialists, and 1 neurologist, were invited to comment. See Online Data Supplement 1 for the list of members.

Methods of Review

In developing the guidelines, we followed recommendations of *The Institute of Medicine's 2011 Clinical Practice Guidelines We Can Trust: Standards for Developing Trustworthy Clinical Practice Guidelines* (*www.iom.edu/cpgstandards*) and graded level of evidence according to published standards (Table 1).[2] Members of the writing committee and invited experts were tasked with making recommendations based on a review of the literature, grading the quality of evidence supporting the recommendations, and assessing the risk–benefit profile for each recommendation. Literature searches were conducted using PubMed, reviewing all articles published since 2000 while including older landmark publications. Original articles and all contributions by committee members and invited experts were made available to each writing committee member. Regular conference calls were held, and brief minutes were circulated via email. Each writing committee member and invited expert was asked to consider every recommendation with regard to class and level of evidence. Controversies were discussed and resolved via email discussions. A final draft was

prepared by the chairmen, Dr. Hussain, and Dr. Blackstone. Writing committee members and invited experts were given a final opportunity to review, comment, and approve the draft before it was submitted to the AATS Guidelines Committee for approval.

Audience, Focus, and Distinguishing Features

Patients with IE are cared for by a team of physicians with expertise in various aspects of the disease. Thus, many guidelines have been produced by societies representing the corresponding specialties. This AATS guidelines document focuses on surgical treatment and perioperative issues: when to operate, how to prepare the patient for operation, how to operate, and other issues relevant to managing and following patients after surgery.[3-8]

Selection, Survival, and Referral Bias

Most studies of IE are affected by selection, survival, and referral bias. Do these biases matter?[9-29] They make it difficult to study the natural history of IE in the general population, because treated and triaged patients enrich the sample seen at regional high-volume centers. Inferences drawn from results of treating such patients are valid for the selected, living, and referred patients, but may not be helpful to the primary care physician who is left without a clear picture of natural history until conservative treatment fails or appears futile, and it becomes clear that the patient must be referred.

So-called “referral bias” represents desirable decisions to consolidate complex care in regional centers of excellence with expertise and experience surpassing that available locally.[29] This is desirable to maximize salvage of patients. It also means that the spectrum of disease seen in these centers will be skewed to the sickest patients,

and physicians and surgeons at these institutions may not appreciate potentially safe and curative conservative therapy for patients with less invasive or curable disease. Given the national trend toward large consolidated hospital systems, combining primary care up to quaternary care, opportunity exists to investigate a more complete spectrum of IE and establish guidelines for its medical management and optimal timing of surgery.

INTRODUCTION

IE is the most severe and potentially devastating complication of heart valve disease, be it native valve endocarditis (NVE), prosthetic valve endocarditis (PVE), or infection on another cardiac device.[3-8] Without treatment, IE is uniformly fatal; the old categories of acute, subacute, and chronic endocarditis referred only to the time it was anticipated to take before the patient died.[30] Even in the current therapeutic era, with appropriate antimicrobial therapy and surgical intervention, multicenter studies report in-hospital mortality of 15% to 20% and 1-year mortality approaching 40%.[11,14,31-49] Patients with valve disease, prosthetic valves, cardiac devices, a history of IE, immune suppression, dialysis, drug abuse, and other medical situations are at increased risk of IE. As a paradoxical effect of advances in medical and surgical therapy, an increasingly elderly population with degenerative heart valve disease, and a rise in staphylococcal infections, the prevalence of IE has increased during the last 30 years. Although it is uncommon for normal valves to become infected, it does happen, especially with *Staphylococcus aureus*. Thus, approximately 50% of IE occurs in patients with no previously diagnosed predisposing cardiac condition.[3,4]

We add to current guidelines from cardiology, infectious disease, and cardiac surgery societies by creating an easy-to-use set of guidelines addressing specific questions of relevance and importance to cardiac surgeons before, during, and after operation.[3-8] The recent American College of Cardiology/American Heart Association (ACC/AHA) guidelines emphasize the importance of an early team approach to patients with IE.[3] The high prevalence of neurologic and other complications requires additional diagnostic and management expertise.[3-7] Patients with IE frequently have comorbidities (often injection drug use in younger patients).[3,4] These comorbidities and primary and secondary infectious foci require diagnostic attention and treatment.

Clinical scenarios presented by patients with IE are often complex.[50-53] IE requires prompt diagnosis for early institution of antibiotic treatment and decision-making related to complications, including risk of embolism and need for and timing of high-risk surgery.[3-7] IE patients require a multispecialty team approach.[3-7] AATS recommends that the IE treatment team include an infectious disease specialist, a cardiologist, and a cardiac surgeon, with input from other specialties such as neurology and nephrology when needed. Execution of the operation, with radical debridement and reconstruction of the heart and heart valves, requires experience and special expertise, yet operations for IE remain associated with the highest mortality of any valve disease.[11,31,32,34,43-46]

Causative microorganism or pathogen, position (aortic, mitral, or right-sided), and type of infected valve (native or prosthetic) are of great importance to pathology and prognosis.[43,45,54] Prosthetic valves can also become infected at the time of valve replacement. Bacteria and fungi have a species-specific repertoire of virulence factors

that allows them to establish and maintain IE. These factors mediate adhesion of the bacteria to endovascular surfaces (e.g., cardiac valves), allow the pathogen to evade the host immune response, and are able to destroy host tissues. Circulating organisms adhere to damaged endothelium of a native or prosthetic valve. The organisms elicit formation of vegetations comprised almost entirely of host cells and proteins, multiply within this "sanctuary site," and produce toxins and enzymes that disintegrate valve tissue and allow extravascular invasion.[54] Severity of invasion and destruction seems to be a function of aggressiveness, virulence, and time, with *S. aureus* being most aggressive and effective.

A great variety of microorganisms can cause IE, and they differ with regard to virulence factors that determine their aggressiveness. The microbiology of IE depends on whether the valve is native or prosthetic and whether the infection is community acquired or healthcare associated (including nosocomial IE).[3-5,7] Staphylococci, streptococci, and enterococci are the most important causative organisms, responsible for approximately 85% of all IE. Staphylococci and streptococci are the most common aggressive and destructive bacteria causing IE. Although *S. aureus* is more common in NVE, *S. epidermidis* is a more common cause of PVE. Fungi form large vegetations or balls, but are usually less invasive, although aspergillus IE is associated with development of mycotic aneurysms and easily becomes disseminated. Pettersson et al. recently described the progression and pathology stages of NVE and PVE in an atlas.[54]

Despite introduction of antimicrobials, IE remains notoriously difficult to treat, and even extended courses of high-dose antimicrobials often fail to cure the infection.[55] Recent research has provided a plausible explanation for this: the biofilm concept.[56]

Biofilm development and quorum sensing are social bacterial behaviors. Bacterial populations live embedded in a self-produced extracellular polysaccharide slime-like matrix, and quorum sensing (a chemical cell-to-cell communication mechanism) synchronizes gene expression and activates assembly and maturation of the biofilm. Once established, biofilm protects bacteria from host immune defenses and impedes antimicrobial efficacy, dramatically reducing the ability of medical therapy alone to eradicate the infection. The capacity for biofilm production is a hallmark of the microorganisms commonly causing IE, including staphylococci, streptococci, and enterococci, but also less common pathogens such as Candida species and *Pseudomonas aeruginosa*.

Tissue disintegration and invasion caused by toxins and enzymes result in serious complications, including heart failure from valve regurgitation or fistulas.[54] Extravascular invasion causes paravalvular abscesses and heart block, and emboli from vegetations cause stroke, mycotic aneurysms, and other related phenomena. Destroyed tissue does not regrow, and valves made leaky by bacterial destruction will continue to leak even if the infection is ultimately eradicated. Stage of the disease at the time of diagnosis is related to pathogen aggressiveness and disease duration.[54]

Outcomes after IE treatment are often related to whether it is a native or prosthetic valve infection. Prosthetic valve infections are generally more invasive and more difficult to treat and cure with antibiotics alone.[43] Formation of a biofilm protecting the organisms represents a biologic basis for the frequent need for surgery for PVE.[56] When comparing aortic and mitral valve IE, aortic valve IE is more invasive (true for both NVE and PVE) and has a higher proportion of prosthetic valve infection.[43] Despite

this, outcomes are worse after surgical treatment of mitral valve IE than aortic valve IE. Three factors contribute to this: 1) mitral valve IE patients have a higher prevalence of comorbidities than aortic IE patients; 2) for invasive IE, the surgical anatomy of mitral valve IE is less favorable; and 3) no allograft valve alternative for severe invasive disease currently exists for the mitral valve.[43] Right-sided IE is typically less invasive, although it is caused by the same aggressive organisms, including *S. aureus*.

Systemic emboli are common in patients with left-sided IE. Embolic strokes, with or without hemorrhagic conversion, are the most frequent and clinically important.[3-5] Although rare, systemic septic emboli can cause mycotic aneurysms in any artery, including the aorta.[3,4] Right-sided IE frequently showers septic emboli to the lungs, leading to development of pulmonary abscesses or empyema if treatment is not instituted early, and can also be responsible for systemic emboli in patients with patent foramen ovale.

All patients diagnosed with IE are first treated with antimicrobials, initially broad spectrum and then adjusted to the sensitivity pattern once it is known.[3-5,7] Antimicrobials to which the organisms are sensitive clear the bacteremia, may prevent or halt further destruction, and, if treatment is initiated early enough, cure the infection. Antimicrobials will, however, not restore the integrity of damaged tissue and valves, and recurrence after a complete course of antibiotics is common.

The hypothesis that IE is a biofilm-associated infection offers plausible explanations as to why endocarditis-related infections are difficult to treat, why recurrence may occur after seemingly successful medical treatment, and why surgery is often required.[56] Surgery effectively disrupts the biofilm, removes vegetations, infected

necrotic tissue, and foreign material, and drains the infected areas, thereby exposing residual live microorganisms and making them vulnerable to antimicrobials and the patient's immune system. In addition, valve repair or replacement restores valve function and cardiac integrity. Nevertheless, final cure is always the result of antimicrobial treatment and the patient's own defense mechanisms.

Many experienced groups are becoming increasingly aggressive in advocating early surgery rather than waiting for complications.[43-46] Kang et al. recently published a randomized study specifically looking at timing of surgery and provided evidence supporting surgery within 48 hours rather than waiting for onset of heart failure or other clinical symptoms.[47] This evolution is based on improved outcomes after surgery and the growing conviction that the penalty for operating on patients with active infection is minimal, and that duration of preoperative antibiotic treatment has no or little effect on outcomes.

In the case of blood-culture-negative IE, surgery can also help to identify the causative microorganism thanks to microbiologic examination of the operative specimen, including molecular testing with polymerase chain reaction (PCR).[57,58]

These new AATS consensus guidelines primarily address questions related to active and suspected active IE affecting valves and intracardiac structures. Management of concomitant device infections is addressed, but not management of isolated infections of devices, including pacemakers, defibrillators, ventricular assist devices, and others. It is understood that surgery is beneficial only if the patient's complications and other comorbidities do not preclude survival and meaningful recovery.

QUESTIONS

Who should care for and operate on patients with IE? (Table 1.1)

Surgery for IE carries the highest risk of any valve surgery, and outcomes differ widely among centers and surgeons. Expeditious diagnosis and institution of adequate treatment require access to substantial expertise in cardiology and infectious diseases. Imaging expertise, particularly in echocardiography, is essential to early diagnosis. Transesophageal echocardiography (TEE) is often needed to diagnose and adequately stage the disease, supplemented selectively by computed tomography (CT) scanning, magnetic resonance imaging (MRI), and positron emission tomography (PET) scanning. Once the diagnosis has been made, the management team should also include a cardiac surgeon and other specialists with the expertise needed to handle complications (e.g., neurologist, psychiatrist, nephrologist). Once surgery is decided on, an anesthesiologist is added to the management team.

The team approach to IE is emphasized in the most recent 2015 AHA/ACC guidelines, and the 2015 European Society of Cardiology (ESC) guidelines recommend that patients with IE should be managed at reference centers by a specialized "endocarditis team."[3-5] Surgical input should be solicited early in the evaluation. When dealing with invasive disease, the surgeon must have enough experience to perform radical debridement and reconstruction and have access to and mastery of the necessary reconstructive procedures.

Diagnosis of IE: What does the surgeon need to know? (Table 1.2)

The diagnosis of IE is based on clinical symptoms, physical findings, microbiology results, echocardiography, and other studies. Duke or modified Duke criteria are used to classify certainty of the diagnosis.[50,52,53]

When IE is suspected, 3 sets of blood cultures should be collected before antibiotics are initiated. At least 2 sets (2 bottles, aerobic and anaerobic) should be obtained immediately from different peripheral sites. An additional set should be obtained a few hours later. Unless the patient is septic, it is reasonable to withhold antibiotics until an adequate number of blood cultures have been collected. Colony-forming units/mL of microbial pathogens do not differ between venous and arterial blood. However, some pathogens require prolonged incubation (*P. acnes*) or special media (histoplasmosis) or are too fastidious to grow in blood culture (*T. whippelli, Coxiella burnetti*, Bartonella species) and require non-culture techniques (e.g., PCR in serum, valve specimens, or paired serologies).

A transthoracic echocardiogram (TTE) must be supplemented with TEE in most cases of suspected prosthetic IE. A TEE should be considered early when organisms with a high likelihood of pyogenic complications are implicated or when there is a question about the presence or absence of valve infection based on the quality of the TTE images. Over the last decade, technological advances have permitted real-time 3-dimensional TEE to provide volumetric data and better morphologic evaluation of cardiac valve leaflets and cusps and the surrounding structures, improving assessment of vegetation size and detection of complications, such as abscesses and valve leaflet or cusp perforations.

Electrocardiogram-gated CT has comparable diagnostic performance to TEE and may be a valuable complement in the preoperative evaluation of patients with aortic PVE. The need for additional imaging will also depend on local availability of such expertise. With the latest generation of multidetector CT (MDCT), the entire heart and thorax can be imaged in just a few heartbeats, and even faster using a dual-source CT scanner. MDCT can be used to detect abscesses and pseudoaneurysms with a diagnostic accuracy similar to TEE, and is possibly superior in providing information about the extent and consequences of any perivalvular extension, including the anatomy of pseudoaneurysms, abscesses, and fistulas.

Promising results have likewise been observed for single-photon emission computed tomography (SPECT) imaging with radiolabeled leukocytes and 18F-fluorodeoxyglucose (FDG) PET-CT imaging in IE. The main added value of these techniques is reduction in misdiagnosed IE, classified as “possible IE” using the Duke criteria, and detection of peripheral embolic and metastatic infectious events. Compared with Duke criteria alone, combined Duke criteria and PET-CT data result in a substantial increase in sensitivity without a loss of specificity.

Although complementary imaging, including MDCT, SPECT, PET-CT, and MRI, appears to be promising, a large multicenter trial is still lacking, and the added value of the additional imaging technologies is yet to be determined.

Once an indication to operate has been established, the surgeon’s focus is on the antimicrobial treatment coverage and the pathology as a determinant of the needed operation. Empiric antimicrobial coverage should be broad enough to cover all likely organisms. If the patient requires urgent surgery when the pathogen and its sensitivity

pattern are unknown, the surgeon and patient must be aware and take this uncertainty into account in calculating the risk and timing of surgery.

Before operation, the surgeon should carefully review the echocardiograms and other imaging studies to better understand the pathology and stage of the disease, which determine the operative approach, especially if invasion is suspected. However, it is important to remember that even TEE is not perfectly accurate, particularly in patients with mechanical valves.

It also needs to be pointed out that the operation itself contributes to the diagnosis. A substantial number of patients with IE go to the operating room before the causative microorganism is identified as either culture negative or before results of the cultures are available. It is critically important that the surgeon secure tissue for microbiologic and histopathologic diagnosis. Even if cultures remain negative, molecular testing with PCR of operative specimens has proven effective in identifying the pathogen, sometimes revising preoperative culture results.

What are the indications for surgery in patients with IE? (Table 2.1)

There is wide agreement about the role of and indications for surgery in patients with IE, and currently there is little to add to the indications. Surgical treatment should be considered in patients with signs of heart failure, severe valve dysfunction, prosthetic PVE, invasion with paravalvular abscess or cardiac fistulas, recurrent systemic embolization, large mobile vegetations, and persistent sepsis despite adequate antibiotic therapy for more than 5 to 7 days.

The ACC/AHA guidelines combine indication and timing and other factors related to complications, primarily neurologic and comorbidities, and other circumstances that

must be considered and weighed in the decision-making process.[3,5] Why and when to operate cannot be separated but must be seen in relation to each other. The final decision to operate should be a consensus decision by the treating team.

If there is any disagreement, it relates to the level of aggressiveness and definition of early surgery. In patients with NVE, heart failure is the most frequent and severe complication; the main question is whether waiting for heart failure symptoms in a patient with severe valve regurgitation offers any benefit (see additional discussion under questions about timing of surgery and duration of preoperative antimicrobials). Approximately half of patients with IE develop severe complications that sooner or later require operation. Early surgery, as advocated by Kang et al. and many other experienced groups, means operating before heart failure has developed and is manifest.[47] In Kang's study, the most frequent complication in the conventional treatment group was embolic stroke. For this reason, once a surgical indication is evident, surgery should not be delayed.

Patients with invasive staphylococcal PVE and early PVE require early surgery. *S. aureus* and *S. lugdunesis* can be very invasive, with metastatic lesions, compared to PVE with coagulase-negative staphylococcus; however, duration of infection before diagnosis and initiation of appropriate antibiotics also influence pathology of IE. Delaying surgery allows destruction to progress and increases the risk of heart block and embolism. For patients with uncomplicated, non-staphylococcal, and late PVE, treatment with antibiotics alone may be worth trying, but often the infection will recur within a few months. When the infected valve is prosthesic, the chance of cure by antimicrobial therapy alone is far less, particularly when the pathogen is aggressive, like

S. aureus. In patients with less aggressive bacteria, e.g., enterococci, vegetations may be miniscule and the infection noninvasive, thus making the diagnosis difficult. The decision about whether and when to replace the valve becomes one based on exclusion of other probable sources of infection.

Surgery to prevent embolism in patients with large mobile vegetations has been a more controversial indication, but the controversy seems to have been resolved. Location, size, and mobility of the vegetation, previous embolism, type of organism, and duration of antimicrobial therapy all influence the associated risk of another embolic event. Large mobile vegetations—greater than 10 mm on the anterior mitral valve leaflet—have been proven to be associated with higher embolic risk. The latest ESC guidelines suggest a vegetation size of 20 mm as an indication for surgery.[4] The trend is to be more aggressive in these cases, because the penalty for operating on patients with active IE is low, and it is frequently possible to preserve the valve, more often the mitral than the aortic valve. There is little logic in waiting for recurrent embolic events that may be devastating.

The general indications may or may not be applicable to right-sided IE. When multiple valves, left- and right-sided, are infected, the indication for surgery is usually the left-sided IE. In right-sided IE, invasion is almost never an issue, but indications for surgery are most often failure to control the infection and septic pulmonary embolism, and less often tricuspid valve regurgitation. Patients with septic pulmonary emboli present with scattered pulmonic infiltrates and abscesses. One consequence of pulmonary embolism is increasing pulmonary vascular resistance and reduced ability to tolerate valve regurgitation, resulting in congestion and right-heart failure symptoms.

Patients with IE are often sick, and development of renal failure is not uncommon. Renal injury can be caused by acute tubular necrosis, antimicrobial drug toxicity, and immune complex–mediated glomerulonephritis.[59] The latter can respond promptly to surgical control of IE, and progressive renal failure can be a reason to move up the operation rather than postpone it.[60] Pathogens causing IE associated with glomerulonephritis include *S. aureus* and *epidermidis* and *Streptococcus viridans*.

The AATS recommendations, although similar, are not identical to the ACC/AHA recommendations.[3,5] Minor changes and nuances have been added. It is assumed that the patient is operable and does not have any contraindication to heparin and cardiopulmonary bypass, e.g., intracranial hemorrhage.

When should the patient undergo operation? (Table 2.2)

The ACC/AHA guidelines define early surgery as surgery "during initial hospitalization independently of completion of a full therapeutic course of antibiotics."[3,5] A common belief is that very few cases of IE are true emergencies requiring same-day surgery.

However, embolic events are completely unpredictable as to timing and severity. For the indication "prevention of embolism," sooner is better, and an argument for same-day surgery can be made. According to Dickerman et al., risk of embolism is highest during the first 2 weeks of antibiotic therapy and is clearly related to size and mobility of the vegetations, although other risk factors exist.[61] The risk of stroke in IE falls dramatically each day after initiation of effective antimicrobial therapy. Reduction in size of vegetations with appropriate antimicrobial therapy also appears to be associated with reduced embolic risk. Surgery undertaken for the prevention of embolism is

therefore mainly relevant early, during the first few days after initiating antimicrobial therapy (emergency or urgent), when the risk of embolism is highest. Several observational studies have identified vegetation length >10 mm as an independent predictor of embolic events or other complications; the risk of embolism in patients with these large lesions is further increased by factors such as severe vegetation moblility, intravenous drug abuse, and staphylcoccal infection.[62-65] When Hubert et al. developed their "embolic risk calculator," vegetation length >10 mm emerged as a key factor.[62] Vegetation length >15 mm has been found to be associated with particularly high risks of IE and death.[63,64] Such studies have been used to include vegetation size as a factor when considering surgery to prevent embolic complications. For example, the newest ESC guidelines recommend urgent surgery for patients with large vegetations (>10 mm) involving the aortic or mitral valve if they have had an embolic event despite appropriate antibiotic treatment or have other complications, such as heart failure, abscess, or persistent infection.[4] Kang et al. demonstrated that patients with large (>10 mm) left-sided vegetations plus severe valve dysfunction benefit from early surgery by conducting a randomized trial in which 37 patients underwent surgery within 48 hours of diagnosis and 39 underwent conventional treatment (with surgery reserved for those who develoved complications or persistent infection).[47] Patients who underwent early surgery had a significantly lower incidence of embolic events than those who received conventional treatment (0 vs. 21%; *P*=.005). It is less clear, however, whether a large left-sided vegetation constitutes an indication for surgery in the absence of embolic events or other complicating factors.

If the patient has prosthetic aortic valve IE with anulus involvement, antimicrobial treatment alone is unlikely to cure the infection and may even fail to prevent progression, leading to damage of the atrioventricular node and conduction system. Once effective antimicrobial therapy has been initiated and an indication for surgery established, delaying the operation may invite and allow new complications.

What is the effect of neurologic complications, embolic stroke, brain hemorrhage, and mycotic aneurysm on indication and timing of surgery? (Table 3.1)

Patients with IE who require surgery but have neurologic symptoms should have a neurologic evaluation and brain imaging, either by CT or MRI, before the planned operation. Imaging should be repeated in case of new or worsening symptoms. The neurologic symptoms, consciousness, location and size of infarct, type (primary or hemorrhagic conversion in infarct), location, size, and timing of hemorrhage, and risk and probability of mycotic aneurysm are all factors to consider when deciding on further imaging, surgery and timing of surgery, and operative risk. An operation using cardiopulmonary bypass will increase swelling of the brain, and heparin may provoke new bleeding.

Because embolic events and strokes are so common in IE patients, routine preoperative screening of asymptomatic patients, particularly those with high-risk vegetations, may be justified. In patients without neurologic symptoms, MRI shows occult cerebral lesions in at least half, most often small ischemic lesions.[66,67] Cerebral MRI has a higher sensitivity than CT in detecting cerebral lesions. Cerebral MRI can also affect the diagnosis of IE by adding 1 minor Duke criterium, and can upgrade the diagnosis in up to 25% of patients presenting initially with non-definite IE, leading to earlier diagnosis.[68]

Current recommendations are that surgery should be delayed for 1 to 2 weeks in patients with non-hemorrhagic strokes, and for 3 to 4 weeks in patients with hemorrhagic strokes. Patients with severe neurologic deficits, unconscious patients, and those unable to follow simple commands should not be operated on until neurologic improvement has been demonstrated and potential for recovery established.

The etiology of intracranial hemorrhage in IE patients includes hemorrhagic conversion of ischemic infarct, pyogenic arteritis, and rupture of mycotic aneurysm. Consequently, the associated risk of another bleed during a heart operation and the safe interval between onset of bleeding and surgery is likely to be specific to each causative etiology. To exclude a mycotic aneurysm, patients with intracranial bleeding must undergo cerebral angiography. However, the yield is low even in patients with bleeding, and indications for angiography are not well established. Presence of a mycotic aneurysm increases the risk of bleeding, and the neurologist and neurosurgeon should decide whether to treat and secure the aneurym before the heart operation.

For those with non-hemorrhagic embolic strokes, the main concerns are worsening the neurologic damage and hemorrhagic conversion of the infarct during operation. The rational for delaying operation is that the risk of worsening neurologic symptoms as a consequence of operation is time related, decreasing with increasing interval from the initial neurologic event. The risk of worsening the stroke symptoms must be weighed against the indications for surgery and the risk of additional emboli during the waiting period. If the patient is stable and risk of additional embolism is deemed to be low, delaying surgery for 1 to 2 weeks is probably beneficial, with repeat brain imaging before operation. However, Barsic et al. found that performing surgery

within 1 to 7 days after an ischemic stroke was not associated with increased in-hospital mortality.[69] The importance of minimal hemorrhagic conversion in an ischemic stroke is yet to be determined. The endocarditis and stroke groups at Cleveland Clinic have agreed on a risk stratification algorithm in patients presenting with aortic or mitral IE: limited stroke <3 cm and no or micro hemorrhage = low risk, acute stroke >3 cm without or with small hemorrhagic conversion = moderate risk, and large acute hemorrhage = high risk (evidence level C).

Should all IE patients scheduled for surgery have preoperative brain imaging? (Table 3.2)

There is no argument about the need for brain imaging in all patients with neurologic deficits. Whether brain imaging should be performed in all IE patients remains controversial. The yield in asymptomatic patients is lower but still significant. Presence of lesions was demonstrated in 35 of 44 brains from cases with proven IE in an autopsy study by Patel et al.[70] Cooper et al. reported detection of brain embolization in 70% of patients in whom clinical evaluation did not reveal a neurologic deficit.[67] Importantly, in their study, mortality seemed to be similar among patients with clinical stroke or with subclinical brain embolization (62% and 53%, respectively), whereas it was significantly lower (12%) in those with a negative MRI. Many centers routinely image the brain with CT or MRI before operation to identify patients who may harbor embolic lesions that could pose a higher risk of intracranial bleeding with heparin administration and cardiopulmonary bypass. Optimal imaging requires use of contrast, with its renal toxicity. If surgery must be delayed to obtain additional imaging, the indication for additional imaging must be weighed against the risk of delaying the operation.

What workup is needed for diagnosing primary infectious focus, secondary manifestations and complications (other than neurologic), and satellite infections in patients with IE? (Table 3.3)

Screening for infected teeth is routine, as is colonoscopy in patients with IE caused by *Streptococcus bovis* (now *S. gallolyticus*).[71-73]

The search for other sources of bacteremia and satellite infections and mycotic aneurysms is guided by symptoms, specific signs, and causing organism. The 2015 AHA Scientific Statement notes the following regarding screening for metastatic foci of infection: "The choice of diagnostic modality or procedure (e.g., CT, MRI, ultrasonography) varies, and the selection should be individualized for each patient (Class I; Level of Evidence C)."[3] There are currently no other recommendations for routinely evaluating all patients with IE for primary or metastatic foci of infection, although many clinicians recommend routine screening for all cases of *S. aureus* IE. Rather, a directed workup is advocated on the basis of localizing signs or symptoms. Patients with aspergillus IE have a higher risk of mycotic aneursyms. In recent years, studies have shown the diagnostic value of other imaging strategies and body imaging in patients with suspected or proven IE in identifying "silent emboli" and helping clinicians stage the "metastatic" lesions that may occur. [74,75] Desch et al. systematically performed whole-body CT scanning on admission in 64 patients and found systemic embolization in 62% (cerebral 36%, splenic 46%, and renal 24%).[74] Basic screening could include ^{18}F-FDG PET/CT of the head, chest, and abdomen.

Spinal infections in patients with IE are important to keep in mind because both entities are associated with hematogenous seeding. In a large series of 606 IE cases, concomitant spondylodiscitis was diagnosed in 28 (4.6%), constituting a third of 91

patients diagnosed with spondylodiscitis during the same period.[76] The organisms implicated in both valvular and spinal seeding are mostly gram-positive bacterial and fungi. The clinical importance of screening patients with spinal infections for IE lies in the fact that oral therapy may be an option for uncomplicated pyogenic vertebral osteomyelitis, whereas it will not suffice for treating IE.

If the IE patient is diagnosed with another infectious focus or abscess, spinal, splenic, or other, the treatment team has to take this into consideration and decide timing of intervention for this versus timing of the heart operation. The scenario with presence of large abscesses requiring immediate intervention is, however, very rare, and there is limited literature on which to base firm recommendations.

How should anticoagulation in patients with IE, with and without stroke or intracranial bleeding, be managed? (Table 3.4)

In itself, IE is not an indication for anticoagulation therapy. The belief that vegetations consist of platelets, cells, and fibrin suggests that anticoagulation could prevent further growth of the vegetations and embolism. Current evidence, however, is to the contrary. The biofilm hypothesis, which suggests that the organisms themselves produce and “build” the vegetations, offers an explanation as to why this is the case.[56] Not only is anticoagulation ineffective in preventing embolism, being on anticoagulation increases the risk of hemorrhagic conversion of an ischemic stroke and brain hemorrhage.

If the patient has a mechanical prosthetic valve or other strong indication for anticoagulation, the treatment team must decide whether anticoagulation is necessary, what to use, and what INR or PTT level to target. There are many scenarios in which compromise is preferable, i.e., less anticoagulation rather than more seems safer. If the

patient has suffered a stroke, any anticoagulation adds to the risk of hemorrhagic conversion, and if bleeding has already occurred, this risk increases even more. Managing a patient with an infected rocking mechanical valve and intracranial bleeding remains a difficult dilemma requiring a consensus team approach to decision-making.

What additional workup is needed just before taking the patient to surgery? (Table 4.1)

The high yield of brain imaging even in patients without obvious neurologic symptoms has already been discussed. When the decision has been made to operate, however, repeat brain imaging may be needed, depending on new neurologic symptoms, interval since the last examination, risk of embolism based on organism, vegetations, and pathology, and whether previous brain imaging demonstrated a stroke or hemorrhage. If the patient has a large stroke(s) and serious neurologic deficit, a neurologist should evaluate the perioperative risk of worsening symptoms and the prognosis and potential for recovery and rehabilitation. In cases with intracranial bleeding, the probability of mycotic aneurysm and need for cerebral angiography should be considered. A formal baseline preoperative neurologic exam should be documented for patients sustaining neurologic injury in the event that further neurologic injury is incurred during and after surgery.

Indications for coronary angiography should follow normal criteria for other surgical conditions. Previous coronary artery bypass grafting is a strong indication. The cardiologist about to perform the coronary catheterization is often justifiably concerned about provoking an embolic event and stroke, and this risk, the risk of worsening renal function with contrast, and the general condition of the patient must be taken into consideration. In patients who are undergoing surgery for aortic valve IE and need

coronary artery evaluation, cardiac CT angiography could be a viable alternative to invasive coronary angiography in assessing coronary artery disease, especially when there are aortic vegetations that may be dislodged during catheterization.

Patients with a history of sternotomy need a preoperative CT of the chest; a CT without contrast provides the best information about cardiac structures and their proximity to the chest wall. For this purpose, MRI does not provide equally precise information. Contrast is not needed unless there are grafts to be localized as well, but in patients with grafts, coronary angiography also provides information about location and mobility of the grafts, indicating adherence or not to the sternum and chest wall.

Is preoperative duration of antibiotic treatment important? (Table 4.2)

Clearing the bacteremia and having the patient on an effective antimicrobial regimen at the time of surgery is important. During the active phase, the operation itself is likely to provoke entry of new bacteria into the bloodstream. Experienced surgeons have operated on patients in whom the organisms turned out to be insensitive to the perioperative antimicrobial regimen, resulting in early relapse and progressive prosthetic valve infection despite changing to an effective regimen within a few days after operation, as soon as the organism and sensitivity were known. It is up to the infectious disease physician on the team to calculate the probability of this happening and advise the surgeon to proceed with the operation or wait for the cultures and sensitivity to be determined if that is possible.

As demonstrated by Mekontso Dessap et al., the probability of positive cultures from explanted valves decreases with duration of preoperative treatment, but reaches its lowest level after 1 week and does not improve further.[77] If a patient has moderate or

severe aortic or mitral regurgitation and an indication for surgery (if he does not have active IE) but is stable, the decision about when to operate is a matter of clinical judgment depending on IE context (NVE versus PVE), stage (noninvasive versus invasive), and pathogen accessibility and sensitivity to antimicrobial treatment. If the patient has NVE, no evidence of invasive disease, and the pathogen is sensitive and responsive to the antimicrobial treatment, the chance of curing the infection is good, and delaying surgery until after a completed course of treatment is reasonable. If, on the other hand, the pathogen is unknown or difficult to treat and evidence of invasion exists, or if the patient has PVE, there is no evidence that delaying surgery to allow a longer period of preoperative treatment is beneficial.

What is the risk of operation for IE? (Table 4.3)

Risk scores specific to IE surgery have been developed from the Society of Thoracic Surgeons (STS) database,[34] and an additional NVE risk score from a single center by De Feo et al.[78] Wang et al. compared the prognostic utility of these contemporary risk scores for mortality and morbidity after IE surgery in 146 patients.[79] The STS IE score and the De Feo et al. NVE score were good predictors of operative mortality after surgery for active IE. Both these and EuroSCORE II were also good discriminators of postoperative morbidities, particularly permanent stroke and prolonged ventilation (>24 hours).

It is important for the infectious disease and cardiology teams first diagnosing and treating these patients to recognize the stage of the disease and the patient's potential need for surgery, and to involve the cardiac surgeon early in the course. Patient comorbidities, disease stage, complications, acuity, as well as surgeon and treatment

team experience, all will affect risk. The risk spectrum is particularly wide in this group of patients. At one end of the spectrum we have the patient who has double PVE, dehisced valves and abscesses, and is septic and very sick; and at the other end is the patient with 1 large mobile vegetation on a native valve without valve dysfunction. The first patient must undergo operation to have any chance of survival. The other patient is presently clinically asymptomatic but at risk of suffering a major embolic event. Surgically, taking the first patient on is a very high-risk, difficult, technical undertaking, while taking the second patient on is a simple low-risk procedure. When the patient is sick in the acute phase, the risk may change hour by hour and often in an unfavorable direction.

SPECIFIC ISSUES RELATED TO CONDUCT OF OPERATIONS FOR ENDOCARDITIS

Intraoperative TEE (Table 5.1)

Echocardiography at the time of surgery is an important diagnostic adjunct in patients with IE and is a Class I recommendation by the American Society of Echocardiography.[80] Because there may be an interval from initial diagnostic imaging to surgery, the findings on intraoperative echocardiography may differ in degree and extent from the original findings. Furthermore, it may be possible to perform a more extensive and detailed study when the patient is fully asleep. It is important that the intraoperative echocardiogram before surgery be comprehensive and use the most advanced technology possible, including 3-dimensional echocardiography when available. A thorough evaluation by an experienced echocardiographer of not only the valve(s) known to be affected, but of all valves, should be performed, because

extension of infection by primary or secondary spread is common and may be overlooked. Abscess and fistula formation and progression in severity of regurgitation should be sought. Findings should be recorded, reported, and discussed with the surgeon performing the operation. Upon completion of operation, a comprehensive echocardiogram should again be performed to detect any important residual pathology or complications and should be video recorded to provide images that serve as a source of comparison should subsequent concerns about relapse or recurrence of infection arise.

Operative approach (Table 5.2)

Sternotomy is usually required for IE operations, because unexpected findings and discovery of more advanced disease than anticipated are common. Good exposure is required for radical debridement.

Surgeons who are comfortable with less invasive operations and experienced enough with IE can approach aortic valve IE via ministernotomy or mitral valve IE via right-sided mini-thoracotomy, but if unsuspected, more advanced, or invasive disease is present, these approaches are likely to provide insufficient exposure.

Removal of infected tissue: Radical debridement (Table 5.3)

When treating infections, it is a fundamental surgical principle to remove infected material, foreign bodies, and necrotic tissue to minimize the residual infectious burden and provide optimal access for host-defense and antimicrobial therapy by surrounding the area with healthy well-vascularized tissue. Because it is easy to overlook pockets of infection, debridement requires good exposure. The surgeon must have an excellent

understanding of the anatomy and pathology and review the TEE in the operating room with an expert echocardiographer. Vegetations, necrotic tissue, and foreign material may hold onto, hide, and protect viable organisms. The biofilm hypothesis offers a good explanation of why its surgical disruption and removal improve the ability of antimicrobials to cure the infection.[56]

Radical debridement means complete removal of foreign material, necrotic tissue, vegetations, and biofilm. “Radical” does not mean excision with wide margins, which may jeopardize valve repair, injure coronaries, cause permanent heart block, and make reconstruction of the heart more difficult.

Infected areas must be opened and unroofed and all infected pockets cleaned out. In patients with PVE, debridement should include removal of the old prosthesis and suture material. Mitral anular calcification is often present in patients with mitral valve IE, and the calcium itself may be the site of infection. In these cases, debridement has to remove infected calcium and expose migrating infection spreading in and along it. However, it must not be so radical that reconstruction is jeopardized. Whenever entering infected areas, having a “dirty” non-cardiotomy suction available is mandatory to avoid contamination of the entire field. Use of cardiotomy suction is avoided until the field is clean to minimize blood contamination.

Debridement is followed by generous irrigation. Many surgeons use local antiseptics and antimicrobials, but no studies specific to IE support the value of this practice. Surgical instruments and gloves should be exchanged after removing all infected tissue and completing irrigation.

Choice of reconstruction and valve replacement: General considerations and recommendations (Table 5.4)

For NVE, and for the mitral valve in particular, the advantage of valve repair over replacement is well documented, although this finding is open to the critique that patients requiring replacement have more advanced disease and are sicker.

For patients requiring valve replacement, there is little evidence that risk of recurrent infection is different between mechanical and tissue prostheses. Several studies have suggested that use of an allograft in patients with aortic valve IE is associated with better survival and lower risk of relapse (no early phase of recurrent infection). Recent publications have questioned the superiority of allografts and highlight its inferior durability compared with alternatives.[81,82] The national trend is to use biologic valves rather than mechanical valves and allografts.[83] However, allografts are still used more often in invasive PVE cases. Also, the Ross operation has been used in selected patients with aortic valve and root IE.

Patients with IE are often very sick and have suffered strokes, so using allografts or bioprosthetic valves simplifies management and avoids postoperative anticoagulation, lowering the risk of hemorrhagic conversion of strokes and other bleeding complications.

Native aortic valve IE (Table 5.5)

For disease confined to the cusps, repair may occasionally be possible. Choice of replacement valve—mechanical or tissue prosthesis—should be based on the usual criteria. When the disease is invasive and the anulus destroyed, reconstruction and usually root replacement are required. For invasive disease, many surgeons believe

that an allograft is a better choice than a prosthetic valved conduit. (This is discussed further under “Prosthetic valve endocarditis.”)

When additional material is needed, autologous pericardium, bovine pericardium, and other material have been used. The choice is according to surgeon preference, but no material has proven superior to autologous pericardium. In patients with invasive aortic valve IE, the destruction most often leaves the left ventricular outflow tract intact, and no additional material is needed.

Prosthetic aortic valve IE (Table 5.6)

Prosthetic valve infections often involve the sewing ring circumferentially, and deeper invasion and destruction can be anywhere around the circumference, but the usual areas are posterior and toward the left under the pulmonary artery or toward the right atrium. Occasionally the sewing ring is infected, but the infection has not yet penetrated deeper and outside the root. When that is the case and the debridement is adequate, it is possible and feasible to implant another prosthetic valve of choice.

More often, though, pockets of infection outside the root need to be opened, unroofed, and debrided. When the infection invades toward the right behind the central fibrous body, it reaches the conduction bundle and the atrioventricular node, and damage to these structures results in heart block. The more extensive and destructive the infection, the stronger is the argument in favor of an allograft over alternative conduits with prosthetic valves. Bioroots, porcine aortic roots, or bovine pericardium roots may also work well if allografts are unavailable. Allograft durability is an issue, maybe even in relation to bioprosthetic roots, but in patients with advanced invasive active IE the primary concern is immediate survival and cure of the infection, and in this

subgroup there is still strong support for use of allografts. Kim et al.[82] and Kirklin[84] question the superiority of allografts for IE based on no difference in mortality and worse durability. The cited studies, however, all report a fairly high mortality. The 3.5% morality for PVE presented by Sabik et al. is yet to be matched.[85] Experience and mastery of the technique used is a condition for good outcomes, and it may be that the surgeon is as important as the choice for reconstruction. Several classic studies have shown that allografts prevent the early hazard phase of relapse, and in a study by Sabik et al., use of an allograft for PVE was associated with medium-term survival comparable to that of patients undergoing operation for aortic valve disease other than IE.[85] Direct comparisons of allografts and other replacement alternatives are difficult because allografts have primarily been used for patients with more invasive and destructive disease. It may also be that greater awareness of the importance of radical debridement has reduced the added benefit of allografts.

Native mitral valve IE (Table 5.7)

Invasive and destructive disease is less common in the mitral than aortic position, and when invasion occurs it is often shallow. When, however, invasion penetrates deeper into the atrioventricular groove, it is much more serious, and radical dedridement and sterilization and drainage of the infected area are more difficult. The surgeon needs to be aware that the ability of echocardiograms, including TEE, to demonstrate invasive disease is less for the mitral valve.

When valve replacement is required, there is no established alternative to prosthetic valves. To anchor the prosthesis, the anulus must be reconstructed. Autologous pericardium and bovine pericardium have been used, as well as

commercially available matrix membranes. No follow-up data are available to indicate the best choice. When available, however, nothing has proved better than autologous pericardium. When reconstructing the mitral anulus and patching entry sites into pseudoaneurysms, patches must be generous to minimize stress on the suture lines. Residual communications beneath the valve into infectious cavities must be avoided. Infected cavities in the atrioventricular groove can be drained to the pericardium or atrium, but most often, neither of these alternatives comes naturally to the surgeon, and the risks associated with both are not well known.

Prosthetic mitral valve IE (Table 5.8)

Differences between the options for native endocarditis and PVE are less obvious for the mitral than the aortic valve. Again, the surgeon must be aware that the ability of TEE to disclose the full extent of the pathology is even worse for PVE, particularly when the prosthesis is mechanical. The main difference is that exposure for debridement and removal of the old prosthesis and suture material is worse than for the aortic valve and left ventricular outflow tract. A dual approach from the left atrium and aorta is often helpful. Again, deep invasion into the atrioventricular groove is uncommon, allowing direct implantation of a new prosthesis without additional reconstruction in most cases. When anulus reconstruction is needed, autologous pericardium, bovine pericardium, and other material have been used. Anchorage to the ventricular muscle to prevent communication and entry into paravalvular cavities beneath the valve is important. Again, repair patches must be generous to minimize tension on the suture lines.

Double valve IE (Table 5.9)

In most cases, IE of both the aortic and mitral valve can be managed in accordance with the recommendations given for each of these valves separately. Destruction of the fibrous structure between the aortic and mitral valves—the intervalvular fibrosa or aorto-mitral curtain—requires reconstruction, and this advanced pathology and the reconstructive surgery have been associated with high risk. Several techniques for performing the reconstruction have been described. These operations are technically demanding, high risk, and require a very experienced valve surgeon.

Right-sided IE (Table 5.10)

The primary objective of surgery for right-sided IE is most often to eliminate the cause of persistent sepsis and a source of septic emboli to the lung, and less often to repair the valve. This means removing infected vegetations and foreign material. Valve repair or replacement is a secondary objective.

Patients with right-sided IE are often injection drug users and poorly compliant patients. For patients with tricuspid valve IE, the best possible repair and preservation of the patient's own valve is the primary choice. If the patient has low or normal pulmonary pressures and low or normal pulmonary vascular resistance, excising the valve and leaving free tricuspid valve regurgitation may allow the patient to survive, but will leave him or her symptomatic with right-sided congestion or even overt right heart failure. If the patient has increased pulmonary pressure and resistance, excising the valve is not advisable.

On the right side of the heart, most surgeons have a preference for bioprosthetic valves, although this preference is not based on any comparative studies. With mechanical valves, access to the right ventricle and pulmonary artery for catheterization and pacemaker leads is lost. The risk of valve thrombosis may be increased on the right side of the heart, because valve irrigation is not as vigorous. Any prosthetic valve in the tricuspid position is associated with increased risk of recurrent IE, particularly in patients who resume injection drug use.

Should regular synthetic vascular grafts or valveless allografts be used when the aorta must be replaced beyond the root? (Table 6.1)

The standard choice is to use a regular synthetic graft to replace the ascending aorta and arch when needed. Many aortic surgeons soak a gel-impregnated graft with rifampin, amphotericin, or aminoglycoside, depending on the organism. The gel binds the antimicrobial in 4 to 6 days. We found no evidence to support this practice. Following the argument that allografts may be more resistant than regular synthetic vascular grafts to reinfection, some surgeons consider it logical to extend an allograft with another valveless allograft, but evidence of benefit is lacking. Using an allograft may make sense if the root has been replaced with an allograft and the field is grossly infected. Extending an allograft into the arch may set up a more difficult reoperation if the allograft has had time to calcify.

Should additional prostheses and vascular grafts not proven to be infected be removed and replaced? (Table 6.2)

A loose vascular graft or one surrounded by pus is infected and should be removed. Often, however, it is not easy to decide if a graft or device is infected.

What is the chance that these other implants are infected even if we see no macroscopic evidence of such? This risk is related to the caustive microorganism and duration of disease and bacteremia. A pragmatic approach is that if it is easy and associated with limited added risk, removing and replacing them is reasonable, whereas if it would be difficult and add importantly to operative risk, those implants could be left alone. If the operation is for mitral PVE, removing an aortic prosthesis may facilitate the operation. The final decisions can be made only by the surgeon at the time of surgery.

When should permanent pacemaker systems be removed in patients undergoing surgery for IE? (Table 6.3)

The answer is easy when the system is infected and in right-sided IE affecting the tricuspid valve, but less clear in the case of left-sided IE and no convincing evidence of pacemaker and lead involvement. In the operating room, leads in the right atrium always have tissue—fibrin and clot deposits around them that are indistinguishable from infective vegetations. We do not have any additional recommendation beyond those given by ACC/AHA.[5] Removal of leads and the pacemaker is reasonable, but adds to complexity postoperatively and to the question of if, when, and how the system should be replaced. Insertion of a new epicardial system in the operating room facilitates postoperative management and is reasonable unless the field is grossly infected. (In the ACC/AHA guidelines, these recommendations are found under "Indications."[5])

Should patients with a known indication for a pacemaker receive a pacemaker system with epicardial leads when undergoing operation for active IE? (Table 6.4)

This question is related to the previous question about removing endocardial pacemaker systems. Epicardial leads are less likely to become infected than transvenous leads, and it is therefore logical to consider placing permanent epicardial

leads at the end of the operation. For patients at increased risk of becoming reinfected, e.g., those on dialysis, injection drug users, or those with ongoing bacteremia at the time of pacemaker removal, such a strategy is even more attractive. Many considerations must be taken into account, including limited venous access, dialysis, pacemaker dependency, and need for left ventricular pacing. However, pacing thresholds may be higher with epicardial leads, causing more rapid draining of the pacemaker power supply. A discussion with an electrophysiologist preoperatively may be wise.

Are there any safety concerns regarding use of mechanical valves in patients with IE? (Table 6.5)

Committing a sick IE patient to anticoagulation adds complexity to postoperative management and increases the risk of bleeding. Intracranial bleeding is the primary concern, but very sick patients are also at increased risk of bleeding from the gastrointestinal tract and other places postoperatively.

Is there any role for local antimicrobials or antiseptics during surgery for IE? (Table 6.6)

Debridement followed by irrigation is included in fundamental surgical principles for managing infections. Irrigation removes residual tissue debris and loose infected material and is an integral part of any valve operation. In addition to normal saline irrigation, many surgeons use local antiseptics and antimicrobials, and some even inject antimicrobials into the tissue around the infected area. There is no evidence for this practice specific to IE, either with regard to benefit or harm.

How should infected areas be drained? (Table 6.7)

Draining the infected area is a fundamental surgical principle for managing infections. For invasive aortic IE, the answer is easy: leaving the infected area open to the pericardium is natural and intuitively better than patching and excluding infected areas and cavities. For mitral valve IE, when there is invasion into the atrioventricular groove, the options are sterilizing the cavity and closing it, allowing it to communicate with the atrium, or allowing communication to the ventricle (risk of aneurysm development) or drainage to the pericardium (risk of bleeding). Allowing communication to the ventricle is the least attractive alternative. Any cavity communicating with the circulation is a potential source of embolism, and if the cavity is communicating with the ventricle, there is risk of a growing pseudoaneurysm. These are difficult decisions for the surgeon, and only she or he can weigh the options and the associated risks and benefits and decide. Awareness of the options and risks provides the best guidance, and treatment is usually individualized based on appearance and the specific technical problems in a given patient.

How should operative specimens be handled? (Table 6.8)

Operative specimens offer another opportunity to identify the pathogen and test its sensitivity to antimicrobials. In blood-culture-negative IE, operative specimens are particularly valuable. Specimens should be handled properly and divided between pathology and microbiology for microscopy and cultures. Pathology, looking for inflammation, neovascularization, and organisms on staining, remains the gold standard for IE (see Von Reyn et al.[86] and Duke criteria).[50,52] Molecular testing with PCR should

be considered whenever there is uncertainty regarding the causative microorganism (see next question). A retrieved embolus may also provide pathogen diagnosis.

What is the role of molecular testing with PCR in identifying pathogens? (Table 6.9)

Identifying the specific pathogen is central to selecting appropriate antimicrobial therapy. Comorbid conditions and the often complicated and prolonged illnesses of patients with IE necessitate careful consideration of culture results before assigning causative status to microorganisms isolated in various cultures. In the case of culture-negative IE, microbial nucleic acid sequencing has been shown to be useful in identifying fastidious microorganisms and non-culturable pathogens (e.g., *Tropheryma whipplei* [agent of Whippel disease], *Coxiella burnetii* [agent of Q fever], and *Bartonella spp.* [agent of cat scratch disease]). Molecular testing involves amplification by PCR, followed by DNA sequencing of any amplified product. Bacterial DNA sequencing may identify the causative microorganism in many cases of IE in which blood and valve cultures have failed. Sequencing cannot provide susceptibility results, but in the future, PCR and sequencing may prove to be the primary test for identifying pathogens in excised cardiac valves.

QUESTIONS RELATED TO POSTOPERATIVE MANAGEMENT

Postoperative antimicrobial treatment and duration? (Table 6.10)

Postoperative antimicrobial treatment and duration should be a decision made in concert with infectious disease specialists using recent guidelines as the general framework.[3,4,7] Standard duration of postoperative intravenous antimicrobial treatment is

6 weeks when the infection is active at the time of surgery, but this may be modified by clinical scenarios. Some have suggested that uncomplicated IE caused by susceptible pathogens can be treated for as little as 2 weeks. It has also been suggested that in patients with IE caused by enterococci, duration of treatment with antimicrobials associated with important harmful side effects, e.g., aminoglycosides, can be shorter or avoided after surgical control of the infection source. Longer duration of treatment may be justified for more invasive infections, difficult-to-treat organisms, or presence of hardware and satellite infections, e.g., osteomyelitis.

For fungal infections, lifelong oral suppression has been suggested. Long term, even lifelong suppression has also been used for vascular graft and other implant infections. The efficiency of these practices is not well studied.

What is the need for follow-up and additional screening for infectious foci that could cause recurrent infection/IE? (Table 7.1)

Postoperatively, we should review patients for probable sources of bacteremia and sanitize those, e.g., sanitation of the teeth and mouth. Patients with IE caused by *Streptococcus gallolyticus* often have colon polyps or colon cancer and should undergo colonoscopy. Repeat echocardiogram before discharge should be routine.

During the first 6 months after surgery, when there is risk of relapse, patients should be followed by an infectious disease specialist. It is unknown whether patients operated on during the active phase of IE before completing their full course of preoperative antimicrobials are at increased risk of recurrent IE.

After 6 months, continued follow-up with a cardiologist is more appropriate. Because of worse tissue quality when the infection is active, after surgery there is increased risk of valve dehiscence, paravalvular leak, and pseudoaneurysm formation,

all good reasons for follow-up echocardiograms to verify healing. Patients are also at increased risk of persistent and recurrent IE. Most patients with IE receive bioprosthetic valves or an allograft with limited durability, so careful long-term follow-up with a cardiologist is important.

Drug abuse is associated with increased risk of relapse and recurrent, difficult-to-cure IE. Rehabilitation, seamless transition of care, and mobilization of social support are essential for any chance of success.

What is the risk of relapse and recurrent IE? (Table 7.2)

Several long-term follow up studies include a diverse population of patients, NVE and PVE in any location, medically and surgically treated patients, and injection drug users, yet still have a limited number of patients. There is, however, no doubt that patients who have been treated for IE have a higher risk of recurrent infection, in the magnitude of 1% to 3% per patient-year.

Often these studies provide limited information about risk of relapse versus recurrence and lack a good description of the follow-up. The microorganism primarily defines relapse versus recurrence: IE caused by the same microorganism suggests relapse, while IE caused by a different microorganism suggests recurrence. We distinguish between early and late infection after implantation of a prosthetic heart valve, with early defined as within 1 year and late as after 1 year or more. Several studies have demonstrated 2 phases, an early hazard phase corresponding to relapse and a longer-term constant phase. One benefit of using allografts for aortic IE has been eliminating the early hazard phase.

QUESTIONS RELATED TO RESIDUAL CONTROVERSIES

Should surgical treatment be offered to injection drug users with IE? (Table 7.3)

Narcotic addiction is a huge public health issue in the United States, and managing IE in these patients is only the tip of the iceberg. It is well documented that injection drug use is associated with IE, particularly right-sided IE. Drug addicted patients are younger on average and most often at low surgical risk; the main issue is high risk of relapse and recurrent IE. Although operative risk is not higher, drug-addicted patients have a higher probability of death in the year following operation than do non-addicted patients.

A major limitation of current medical care for injection drug users is that appropriate treatment for addiction is very difficult to access because of a lack of providers and facilities and lack of insurance and other means to pay for the scarce resources that may be available. Injection drug use is a very serious comorbidity that must be included and weighed in decision-making and be treated, mobilizing and taking advantage of all available resources and options for drug rehabilitation.

Should surgical treatment be offered to IE patients on dialysis? (Table 7.4)

Patients on dialysis are 10 to 18 times more likely to develop IE than the general population, and their operative risk is higher and long-term outcomes worse than for patients who are not on dialysis. Nevertheless, it is reasonable to offer surgery when the additional burden of comorbidities is not overwhelming.

Patients in renal failure will calcify biologic implants faster than patients with good renal function, an argument used for avoiding such implants. Choice of valve, however, must be seen in the context of anticipated longevity of the patient and be weighed

against the risks associated with use of a mechanical prosthesis and anticoagulation in a given patient. In support of this conclusion, several studies, including one devoted to IE, demonstrate that survival of patients on dialysis after valve surgery is not affected by valve choice.

Should surgical treatment be offered to IE patients with liver cirrhosis? (Table 7.5)

Liver cirrhosis is a risk factor for IE. In a recent multicenter Spanish study, nearly 10% of IE patients had liver cirrhosis.[87] The importance of this comorbidity should be weighed in decision-making. The added operative risk associated with liver cirrhosis is related to its severity, as accessed by the Child-Pugh or MELD score.

Who should get antibiotic prophylaxis for IE? (Table 7.6)

Current guidelines recommend restricting prophylaxis to the highest risk patients, defined as those with the highest incidence of IE or highest risk of adverse outcomes from IE.[3,4] Patients at highest risk include those with prosthetic valves, previous IE, cyanotic congenital heart disease, and congenital heart disease repaired with prosthetic material. Antibiotic prophylaxis is not recommended for other forms of valvular or congenital heart disease.

As per AHA guidelines,[3] evidence for prophylaxis has been found to be reasonable only for dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of the teeth, or perforation of the oral mucosa. In the case of other prosthetic material (excluding surgically created palliative systemic pulmonary shunts or conduits), such as anuloplasty rings, neochords, atrial septal closure devices, and mitral valve repair clips, there have been only sporadic case

reports of infected devices. Given the low prevalence of infection and scarcity of data, there is no definitive evidence that prophylaxis in these patients is warranted.

The NICE (National Institute for Health and Care Excellence, United Kingdom) guidelines[88] take an even more radical departure from the previous prophylaxis standards in not recommending antibiotic prophylaxis for dental or non-dental procedures (e.g., respiratory, gastrointestinal, and genitourinary).

A surgical aspect to weigh is the consequences of another episode of IE. It will be higher risk and more devastating the more previous operations and the more prosthetic material the patient has in the heart.

How should patients with remote IE be managed? (Table 7.7)

Patients with valvular disease and a history of endocarditis or treated and healed IE should be treated on the merits of their functional deficit. These patients are at higher risk of IE, but whether that risk is high enough to affect decision-making is unclear. We identified no study devoted to remote IE, but many studies in which remote or healed IE cases were included. Early after a complete course of treatment there may be uncertainty about residual infection. Whenever that is the case, it is important to carefully examine the operative specimens for inflammation and residual bacteria. The findings will guide additional antimicrobial treatment.

IDENTIFIED KNOWLEDGE GAPS

For each recommendation the wording and level of evidence express the certainty inviting further research. In this section, we highlight a few that we believe are particularly important at this point in time.

1. Studies of timing of surgery for IE in patients with neurologic complications have so far not provided clear answers to optimal timing and risk stratification. These patients are at risk of complications not only during surgery, but also before and after. Studies of the impact of intracranial bleeding on risk of open heart surgery related to symptoms (symptomatic, asymptomatic), context (primary bleed, hemorrhagic conversion of ischemic stroke), size of the bleed (micro, small, large), and so on, should allow better assessment of risk. Because benefits of early surgery have been widely recognized, the current trend is to offer earlier surgery to patients with neurologic complications.

2. Risk of embolism has remained a somewhat controversial indication for surgery and deserves additional studies. Kang et al. showed that the main advantage of earlier surgery was prevention of embolic events, but this did not affect short-term survival.[47] Present indications focus on the size, mobility, and location of vegetations, but vegetations are not the only source of embolism. Although logic suggests immediate surgery for this indication, supporting data are still insufficient. Additional studies of new events, complications, and pathology progression occurring during the interval between diagnosis and operation are needed.

1029

1030 **3.** Imaging is still not perfect, particularly for mitral valve PVE, and there is more to
1031 learn about new imaging modalities. Improved and more precise diagnosis of
1032 invasive disease and advanced pathology are desirable for planning the operation
1033 and assessing the need for complex reconstruction. This will also allow better
1034 assessment of risk and prognosis.

1035

1036 **4.** Good contemporary studies of risk of relapse and recurrence in the era of earlier
1037 surgical interventions during the active phase of IE are needed. Recent studies
1038 have questioned whether allografts truly are better than prosthetic valves and
1039 conduits for any patient with IE.

1040

1041 **5.** Studies specific to IE of the possible benefits of local antiseptics and antimicrobials
1042 are lacking.

1043

1044 **6.** Information about the spectrum of infections, pathogens, and associated
1045 pathologies after implantation of transcatheter valves and other transcatheter
1046 devices is sparse. There are reports of an increased occurrence of IE after
1047 implantation of percutaneous prosthetic valves in the pulmonic position; these valve
1048 infections seem to respond well to antimicrobial treatment.

1049

1050 **7.** Patients with a history of IE or remote IE present in different ways. Most show up
1051 with functional valve issues after the active infection has been cured with

antimicrobials, and some have signs of invasive pathology with pseudoaneurysm and cavities. Long-term risks associated with these lesions are not well studied, and indications for intervention beyond those normally applicable to valve dysfunction have not been defined.

TABLE 1. Team Approach to Patients with IE

Recommendations	COR	LOE	References
1. Who should care for and operate on patients with IE?			
Patients with suspected IE should ideally be cared for at centers with access to a complete team, including cardiology, infectious disease, cardiac surgery, and other services needed to handle IE complications	I	B	4,5,7,89
Surgeons operating on patients with IE should be well-trained, experienced valve surgeons who are well versed in the different reconstruction techniques needed by patients with advanced disease	I	C	4,5,31,89
2. Diagnosis of IE: What does the surgeon need to know?			
At the time of surgery the patient should be on an effective antimicrobial regimen (correct dosage and route of administration) to which the causative microorganism is sensitive, or be broadly covered when organism and sensitivity are unknown.	I	B	3-5,7,55,58
For surgery planning, the surgeon should have the best possible understanding of the pathology. This will usually require advanced imaging techniques, such as TEE	I	B	3-5,7,90-98
Use of imaging modalities other than echocardiography may also be appropriate in selected cases	IIb	C	3-5,95,99-103

1062 **TABLE 2. Indications For, and Timing Of, Surgery for Patients with IE**
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Recommendations	COR	LOE	References
1. What are the indications for surgery in patients with IE?			
Surgery during initial hospitalization independently of the completion of a full therapeutic course of antibiotics is indicated in patients with IE who present with valve dysfunction resulting in symptoms of heart failure	**I**	**B**	3-7,9,11,46,104-114
Surgery during initial hospitalization independently of the completion of a full therapeutic course of antibiotics is indicated in patients with left-sided IE caused by *S. aureus,* fungal, or other highly resistant microorganisms	**I**	**B**	3-5,7,9,18,31,40,105,110,115-121
Surgery during initial hospitalization independently of completion of a full therapeutic course of antibiotics is indicated in patients with IE complicated by heart block, anular or aortic abscess, or destructive penetrating lesions	**I**	**B**	3-7,11,43,85,105,106,108-110,122-129
Surgery during initial hospitalization independently of completion of a full therapeutic course of antibiotics for IE is indicated in patients with evidence of persistent infection as manifested by persistent bacteremia or fever lasting longer than 5 to 7 days after initiation of appropriate antimicrobial therapy	**I**	**B**	3-5,7,45,105,106,110,118,120,130
Surgery is recommended for patients with PVE and relapsing infection (defined as recurrence of bacteremia after a complete course of appropriate antibiotics and subsequently negative blood cultures) without other identifiable source for portal of infection	**IIa**	**C**	106
Surgery during initial hospitalization independently of the completion of a full therapeutic course of antibiotics is reasonable in patients with IE who present with recurrent emboli and persistent vegetations despite appropriate antibiotic therapy	**IIa**	**B**	3-6,47,61,63,91,131-134
Urgent or even emergency surgery may be considered in patients with NVE or PVE who exhibit mobile vegetations greater than 10 mm in length with clinical evidence of embolic phenomena despite appropriate antimicrobial treatment	**IIb**	**B**	31,47,63,91,135
In patients with right-sided IE, surgery should be considered for NVE or PVE when large vegetations are present and there is evidence of persistent infection manifested by persistent bacteremia or fevers lasting longer than 5 to 7 days after initiation of appropriate antimicrobial therapy, or in those with evidence of septic pulmonary embolism	**IIb**	**B**	4,7,136

Recommendations	COR	LOE	References
2. When should the patient undergo operation?			
Once an indication for surgery is established, the patient should be operated on within days	**I**	**B**	3-6
Earlier surgery (emergency or within 48 hours) is reasonable for patients with large mobile vegetations at imminent risk of embolism	**IIa**	**B**	3-6,46,62,133,137,138
In patients with stroke and neurologic deficits, timing is decided by weighing the need for cardiac surgery against the risk of expanding the stroke or provoking intracranial bleeding during the operation (see specific question about neurologic complications)	**IIa**	**B**	3-6,33,61-63,67,69,104,108,110,125,137,139-154

1068 **TABLE 3. Pre-Surgical Work-Up and Management of Patients with IE**
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Recommendations	COR	LOE	References
1. What is the effect of neurologic complications, embolic stroke, brain hemorrhage, and mycotic aneurysm on indication and timing of surgery?			
If a cerebral mycotic aneurysm has been diagnosed, treatment and follow-up of the patient should be in close collaboration with neurologic and neurosurgery expertise	I	C	3,4,6,155
In patients with a recent intracranial hemorrhage, a delay of operation for 3 or more weeks is reasonable	IIa	B	3-6,138,141,156-159
Earlier surgery is reasonable for patients with non-hemorrhagic strokes and a strong cardiac indication for urgent surgery	IIa	B	3-6,69,157,160-162
Patients with large and multiple strokes and severe neurologic symptoms should be carefully evaluated by a neurologist before being offered surgery	I	B	3,4,6
For patients with IE and neurologic symptoms and significant intracranial hemorrhage, angiography should be considered to rule out mycotic aneurysm	IIa	B	3,4,6,155
2. Should all IE patients scheduled for surgery have preoperative brain imaging?			
Endocarditis patients with neurologic symptoms should have brain imaging	I	B	3,4,6
It is reasonable to screen patients with left-sided IE for possible stroke or intracranial bleeding before operation, particularly if they have cardiac lesions considered high risk for embolic events	IIa	B	66-68,70
3. What workup is needed for diagnosing primary infectious focus, secondary manifestations and complications (other than neurologic), and satellite infections in patients with IE?			
Patients with IE should be screened for primary noncardiac focus of infection, noncardiac complications, and satellite infections: The choice of diagnostic procedure (e.g., CT, MRI, ultrasonography) varies, and the selection should be individualized for each patient based on clinical symptoms and suspicions	I	C	3,4
4. How should anticoagulation in patients with IE, with and without stroke or intracranial bleeding, be managed?			
Anticoagulation management in patients who have compelling indications for anticoagulation, e.g., atrial fibrillation, mechanical prosthetic valve, deep vein thrombosis, or pulmonary embolism, has to seek compromises, taking all risks and benefits into consideration	I	C	163-176

Recommendations	COR	LOE	References
Heparin should be used cautiously in all patients with IE, particularly when there is evidence of brain hemorrhage, and be temporarily withheld in patients with higher risk of rebleed	I	B	4,164

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TABLE 4. Additional Work-Up, Preoperative Antibiotics, and Risk of Operation for Patients with IE

Recommendations	COR	LOE	References
1. What additional workup is needed just before taking the patient to surgery?			
When surgery is decided upon, before going to the operating room, it is reasonable to obtain brain imaging or repeat brain imaging	IIa	B	67,68,70
The need for preoperative coronary angiography should be guided by normal criteria. This is particularly important if the patient has had coronary artery bypass grafting. In patients with large aortic valve vegetations, CT angiography is an alternative to assess the coronary arteries	I	C	3,4,6,177
When repeat sternotomy is required, computed tomography of the chest is recommended when possible to assess risk of sternal reentry	IIa	C	178
2. Is preoperative duration of antibiotic treatment important?			
The patient should be on an effective antimicrobial regimen at the time of surgery. Ideally, the sensitivity of the causative organism is known	I	B	3-5,7,55,58
Once the patient is on an effective antimicrobial regimen, further delay of surgery is unlikely to be beneficial.	IIa	B	3-5,7,77,104,110,125,179-181
3. What is the risk of operation for IE?			
The patient should be quoted a risk, taking into consideration all factors known to affect the risk of the operation	I	C	34,78,79,182

TABLE 5. General Features of Intraoperative Management of Patients with IE

Recommendations	COR	LOE	References
1. Intraoperative TEE			
Intraoperative TEE is mandatory when performing surgery for IE	I	B	3-5,80,90,97,183-187
2. Operative approach			
Medium sternotomy is the recommended approach, with few exceptions	I	C	
3. Removal of infected tissue: Radical debridement			
All infected and necrotic tissue and foreign material should be radically debrided and removed	I	B	43,85
4. Choice of reconstruction and valve replacement: General considerations and recommendations			
For patients with NVE and infection limited to the valve cusps or leaflets, repair is performed whenever possible	I	B	3-6,43,152,188-198
When simple valve replacement is required, choice of valve—mechanical or tissue prosthesis—should be based on normal criteria: age, life expectancy, comorbidities, and expected compliance with anticoagulation	I	B	4-6,197,199-201
It is reasonable to avoid use of mechanical prostheses in patients with any intracranial bleeding or those who have suffered a major stroke	IIa	C	
For patients with invasive disease and destruction, reconstruction should depend on the involved valve, severity of destruction, and available options for cardiac reconstruction	I	B	6,43,44,85,111,202,203
5. Native aortic valve IE			
For patients with native aortic valve IE and infection limited to the valve cusps, repair may occasionally be possible. Choice of replacement valve—mechanical or tissue prosthesis—should be based on usual criteria	I	B	4-6,43,83,197-201
For invasive and destructive native aortic valve IE requiring root reconstruction and replacement, using an allograft may be beneficial, but a prosthetic bioroot or prosthetic valved conduit with a mechanical or bioprosthetic valve are acceptable alternatives, with choice guided by surgeon training and experience.	IIa	B	6,8,44,81,82,199,200,204-208

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Recommendations	COR	LOE	References
6. Prosthetic aortic valve IE			
If the root and the anulus are preserved after radical debridement, it is reasonable to implant a new prosthetic valve—mechanical or tissue—based on normal criteria	**IIa**	**B**	6,44
If there is anulus destruction and invasion outside the aortic root and root reconstruction and replacement is required, an allograft or a biologic tissue root is preferable to a prosthetic valved conduit	**IIa**	**B**	6,8,44,81-83,85,200,202,204,206-217
7. Native mitral valve IE			
Mitral valve repair is the preferred choice whenever possible, including use of a prosthetic anuloplasty ring when appropriate	**I**	**B**	43,152,188-196
When valve replacement is required, a new prosthetic valve, mechanical or tissue, is acceptable, unless there is risk of intracranial bleeding, in which case a tissue valve is preferred	**IIa**	**B**	4-6,199,201
When there is anulus destruction and invasion, the mitral anulus is reconstructed and the valve prosthesis anchored to the ventricular muscle or to the reconstruction patch in a way that prevents leakage and pseudoaneurysm development beneath the prosthesis	**IIa**	**B**	43,188,192,203
8. Prosthetic mitral valve IE			
A new prosthetic mitral valve, mechanical or tissue, is acceptable, unless there is risk of intracranial bleeding, in which case a tissue valve is preferred	**IIa**	**B**	4-6,43,199,201,203
When there is anulus destruction and invasion, the mitral anulus is reconstructed and the valve prosthesis anchored to the ventricular muscle or to the reconstruction patch in a way that prevents leakage and pseudoaneurysm development beneath the prosthesis	**IIa**	**B**	43,203,218
9. Double valve IE			
If the aortic root and aortic and mitral anuli are preserved after radical debridement, it is reasonable to implant mechanical or biologic valves, with the choice based on normal criteria	**IIa**	**B**	6,219,220

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Recommendations	COR	LOE	References
If there is aortic anulus destruction and invasion, and root reconstruction and replacement is required, an allograft or bioroot may be preferable to a prosthetic valved conduit, and if the mitral anulus shows invasion and destruction, it should be reconstructed to anchor the valve prosthesis to the ventricular muscle or to the anulus reconstruction patch to avoid leakage and pseudoaneurysm development beneath the prosthesis	IIa	B	124,126,219-224
Infection destroying the intervalvular fibrosa requires reconstruction of this structure, and it is preferable that surgeons taking on these cases master such techniques	IIa	C	219,223,225-229
10. Right-sided IE			
The primary objective of surgery for right-sided IE is radical debridement of infected vegetations and foreign material	I	B	57,136,201,230-242
Tricuspid valve repair should be attempted whenever possible	I	B	136,230-233,235,243,244

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TABLE 6. Specific Considerations in Surgical Management of Patients with IE

Recommendations	COR	LOE	References
1. Should regular synthetic vascular grafts or valveless allografts be used when the aorta must be replaced beyond the root?			
When distal ascending aorta, hemiarch, or arch replacement is required, a synthetic graft is the standard choice, but a valveless allograft is an alternative in an infected field for replacing the ascending aorta beyond the root	IIb	B	127,245
2. Should additional prostheses and vascular grafts not proved to be infected be removed and replaced?			
Inspection and removal of additional prostheses and vascular grafts, even if not proven to be infected, should be considered and is reasonable if the causative microorganism is *S. aureus* or fungus, provided that the added difficulty and risk is not prohibitive	IIa	C	127,246-249
3. When should permanent pacemaker systems be removed in patients undergoing surgery for IE?			
Complete removal of pacemaker or defibrillator systems, including all leads and the generator, is indicated as part of the early management plan in patients with IE and likely infection of the device or leads	I	B	4,5,250-257
Complete removal of pacemaker or defibrillator systems, including all leads and the generator, is reasonable in patients with right- or left-sided valvular IE caused by *S. aureus* or fungi, even without evidence of device or lead infection	IIa	B	4,5,250,252-258
Complete removal of pacemaker or defibrillator systems, including all leads and the generator, is reasonable in patients undergoing surgery for valvular IE caused by any organism	IIb	C	4,5,256
4. Should patients with a known indication for a pacemaker receive a pacemaker system with epicardial leads when undergoing operation for active IE?			
At the time of surgery for IE, implantation of a new pacemaker system with epicardial leads may be considered when the patient is pacer dependent and has effective antimicrobial coverage	IIb	C	

Recommendations	COR	LOE	References
5. Are there any safety concerns regarding use of mechanical valves in patients with IE?			
Mechanical valves should be avoided in patients with IE and evidence of intracranial bleeding or large brain infarcts, and in patients who are very sick and anticipated to have a prolonged postoperative course	I	C	164
6. Is there any role for local antibiotics or antiseptics during surgery for IE?			
After completed debridement, generous irrigation of the surgical field with normal saline is recommended	I	C	
7. How should infected areas be drained?			
Whenever feasible, leaving infected areas open to the circulation or the pericardium is optimal from the standpoint of treating the infection	IIb	C	43
8. How should operative specimens be handled?			
Operative specimens should be secured for examination by the pathologist to determine presence of organisms and inflammatory activity	I	B	4,7,86,259
Operative specimens should be used for microbiologic and molecular testing to identify or confirm the pathogens and their sensitivity to antimicrobial therapy	I	A	4,7,58,86,259,260
9. What is the role of molecular testing with PCR in identifying pathogens?			
Whenever there is clinical suspicion of IE and doubt about the causative organism, molecular testing can be useful to identify and confirm the pathogens or causative organisms in the operative specimens	IIa	B	4,7,31,58,259-264
10. What postoperative antimicrobial treatment is required, and for how long should the patient be treated?			
When perioperative cultures and organism sensitivity are known, the antimicrobial regimen and duration of treatment are reconsidered and decided upon	I	B	3,4,7
After surgery for active IE, standard duration of postoperative intravenous antimicrobial treatment is 6 weeks, counted from the day of surgery, but regimen and duration may be modified and adjusted depending on the organism and its sensitivity to antimicrobials, treatment response, and pathology	IIa	B	3,4,7,265,266
For fungal IE, lifelong oral suppressive therapy is reasonable	IIa	B	3,4,7

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1093 **TABLE 7. Surveillance and Special Considerations for Patients with IE**

Recommendations	COR	LOE	References
1. What is the need for follow-up and additional screening for infectious foci that could cause recurrent infection/IE?			
Primary infectious focus and microorganism portal of entry must be treated during or just after the IE episode, including follow-up and screening for underlying infectious foci and morbidities	I	B	3,4,7
IE caused by *Streptococcus gallolyticus* is an indication for colonoscopy within a reasonable time after operation	I	B	3,4,71,72,267-270
Patients with a history of injection drug use should be treated for their addiction	I	B	3,4,57,242
After surgery for IE, eradication of the pathogen is essential and should be verified by follow-up for 6 months with an infectious disease specialist	I	C	3
After valve surgery for IE, cure of the infection should be documented by echocardiogram, and the patient should follow up with a cardiologist	I	C	3
2. What is the risk of relapse and recurrent IE?			
Patients who have undergone surgery for IE should be informed about the increased risk of recurrent IE and the need for prophylaxis	I	B	3,179,200,271-277
3. Should surgical treatment be offered to injection drug users with IE?			
Normal indications for surgery are reasonable to apply to patients who are intravenous drug users. Decision-making must take the addiction into account, and management must include treatment of the addiction	IIa	C	3,4,7,57,201,238,242,278
4. Should surgical treatment be offered to IE patients on dialysis?			
Normal indications for surgery are also reasonable to apply to patients on dialysis, but their additional comorbidity must be factored into their risk and outcome assessment	IIa	C	279-285
Patients with renal failure have shorter durability of bioprostheses and allografts because of early calcification, and this may be considered in the choice of an allograft or a bioprosthesis versus a mechanical valve	IIa	B	280,281
5. Should surgical treatment be offered to IE patients with liver cirrhosis?			
Normal indications for surgery are reasonable to apply to patients with liver cirrhosis, but their additional comorbidity must be factored into their risk and outcome assessment	IIa	C	87,286,287

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Recommendations	COR	LOE	References
6. Who should get antibiotic prophylaxis for IE?			
Patients who have undergone surgery for IE constitute a high-risk group for recurrent IE and should be recommended for IE prophylaxis according to guidelines	**IIb**	**B**	3-5,88,288
7. How should patients with remote IE be managed?			
Normal indications for valve repair or replacement apply to patients with healed or remote IE, but conditions predisposing for IE should be diagnosed and treated	**I**	**C**	

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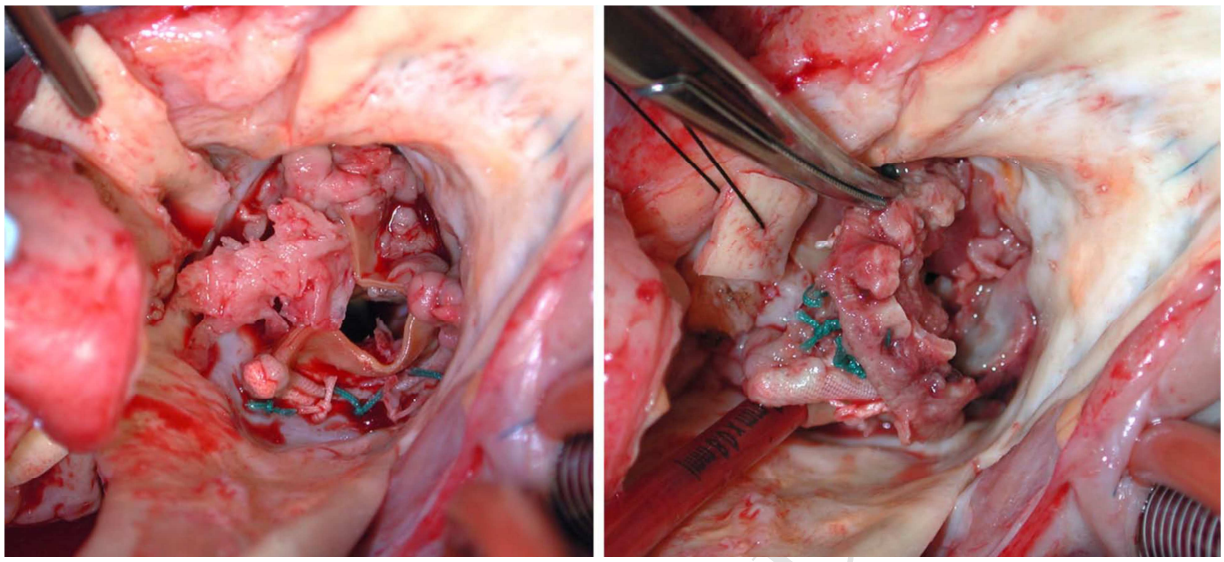
CENTRAL FIGURE



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Legend. Vegetation and dehiscence in prosthetic valve endocarditis—a surgical disease

CENTRAL MESSAGE

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These guidelines describe diagnosis, indications, timing, surgical treatment, and perioperative care for patients with infective endocarditis, and early surgeon involvement in team decision-making