ANESTHESIOLOGY

Anesthesia Considerations in Infective Endocarditis

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ABSTRACT

The management of infective endocarditis is complex and inherently requires multidisciplinary cooperation. About half of all patients diagnosed with infective endocarditis will meet the criteria to undergo cardiac surgery, which regularly takes place in urgent or emergency settings. The pathophysiology and clinical presentation of infective endocarditis make it a unique disorder within cardiac surgery that warrants a thorough understanding of specific characteristics in the perioperative period. This includes, among others, echocardiography, coagulation, bleeding management, or treatment of organ dysfunction. In this narrative review article, the authors summarize the current knowledge on infective endocarditis relevant for the clinical anesthesiologist in perioperative management of respective patients. Furthermore, the authors advocate for the anesthesiologist to become a structural member of the endocarditis team.

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Infective endocarditis is a (predominantly bacterial) infection of a native or prosthetic heart valve, or of the cardiac endocardial surface. Even though it is a fairly rare disease affecting only approximately 3 to 15 per 100,000 people per year,[1] the incidence of infective endocarditis is increasing,[2] and despite all advances in medical treatment, mortality is still as high as 20% in hospital and about 30% after 1 yr.[3] Cardiac risk factors and microbiologic profiles for infective endocarditis vary worldwide: while rheumatic valve disease is the most common risk factor in developing countries, congenital or degenerative valvular disease, prosthetic valves, or cardiovascular implantable electronic devices represent the most relevant risk factors in the developed world. Noncardiac risk factors comprise IV drug use; indwelling intravascular devices and catheters, *e.g.*, for hemodialysis; compromised immunity; or cancer.[4]

Endocarditis primarily involves the heart valves, but can also affect the mural endocardium in the presence of a regurgitant jet due to valve insufficiency. In brief, the pathogenesis of infective endocarditis can be divided into distinct phases: after pathogens have gained access to the bloodstream (*bacteremia*), they attach to damaged or inflamed cardiac endothelial surface and colonize valve tissue (*adhesion*).[5] Consecutively, platelets and fibrin are recruited to create an endocarditis vegetation (*proliferation*), and subsequently biofilm formation occurs.[6] With progression of the disease, the infection may cause structural damage to surrounding cardiac tissue, and the vegetation can lead to septic embolization in other organs, mainly brain, kidneys, and skin (*dissemination*; fig. 1).[7]

Knowledge on diagnosis and clinical management of infective endocarditis has been reviewed before,[2,8] and comprehensive treatment guidelines are available from various societies.[9–13] In all these guidelines and recommendations, the mainstay of the management of infective endocarditis is early diagnosis based on physical examination, imaging, and microbiologic studies according to the modified Duke criteria.[14]

Infective endocarditis is a challenging clinical condition with a strikingly high morbidity and mortality, requiring a multidisciplinary approach to urgent decision-making. About half of patients with infective endocarditis fulfil the criteria to undergo surgery, adding up to about 25,000 surgical cases per year in the United States alone.[3,15] In the perioperative period, the (cardiac) anesthesiologist plays a significant role in treatment of patients with infective endocarditis. However, literature specifically on perioperative care in patients undergoing surgery for infective endocarditis is scarce. The aim of this narrative review is to summarize current knowledge on infective endocarditis relevant to perioperative anesthesia management.

Preoperative Care

Early diagnosis is key to a successful treatment of infective endocarditis. Here, diagnosis first requires initial clinical suspicion, based on clinical presentation and risk factors. Infective endocarditis usually presents with rather nonspecific signs and symptoms, with fever and malaise being the most common ones.[2] Clinical suspicion should then be followed by evaluation according to the modified Duke criteria,[14] which still represent the accepted standard concerning diagnostic strategy, with high sensitivity and specificity for infective endocarditis[7]: blood culture is the pivotal laboratory test. Most patients with infective endocarditis will have a positive blood culture,[16] representing a major or minor criterion according to the Duke criteria. Echocardiography

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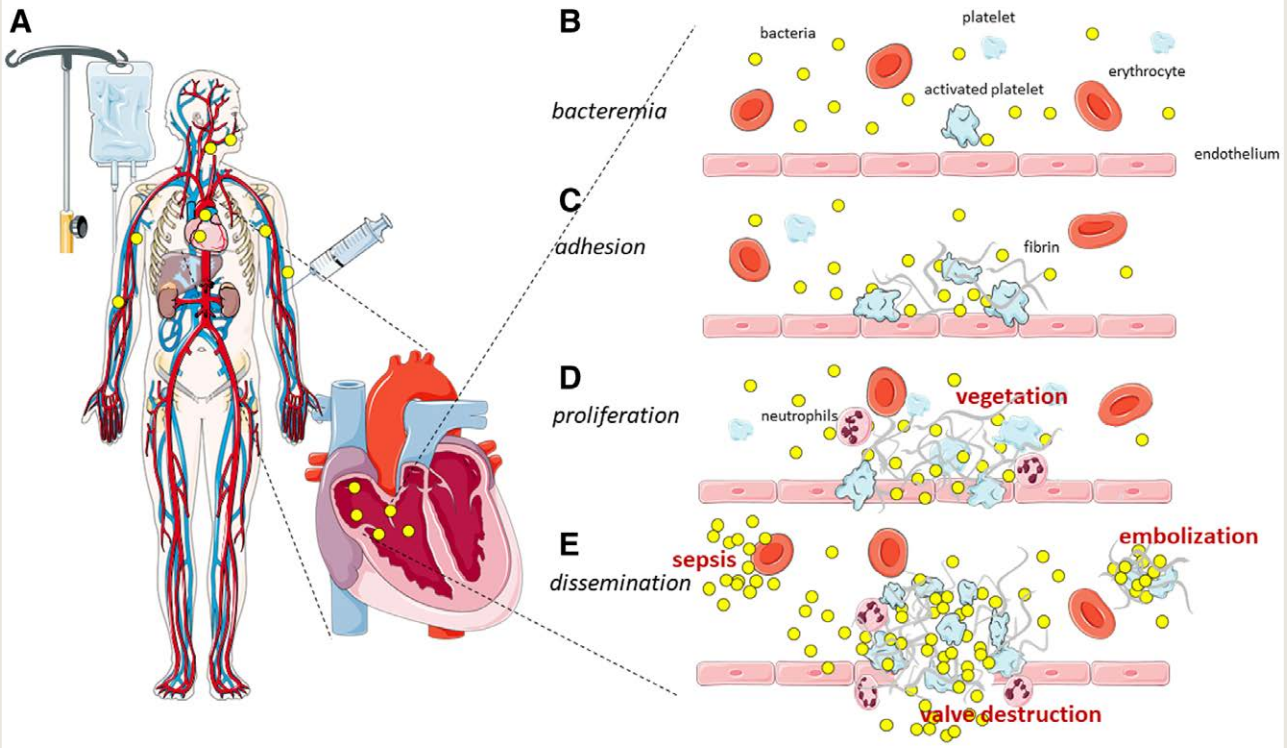

Fig. 1. Pathophysiology of infective endocarditis.[6] After entering the blood stream *via, e.g.*, the oral route, indwelling catheters, or intravenous drug injection (*A*), leading to *bacteremia* (*B*), pathogens accomplish *adhesion* to the (inflamed or damaged) cardiac valve endothelium (*C*). *Proliferation* of the pathogens on the valve by recruitment of activated platelets and fibrin leads to maturation of the vegetation (*D*). Eventually, *dissemination* of the infectious thrombus can lead to cardiac valve destruction, embolization, and sepsis. Adapted from Werdan *et al.*[5] Reprinted with permission from Springer Nature.

is the initial imaging technique of choice (fig. 2), in selected cases supplemented by nuclear cardiac imaging or cardiac computed tomographic angiography.[9]

Generally, the management of infective endocarditis aims at the eradication of the infection and the restoration of cardiac structures to prevent local and systemic complications. Once infective endocarditis is suspected, empiric bactericidal antibiotic therapy should be initiated as soon as possible, according to published guidelines,[9,10] and/or consultation of a microbiologist and infectious disease specialist.

Subsequently, close monitoring for the effectiveness of treatment, the potential occurrence of complications, and indication for surgery is strongly recommended. A multidisciplinary team should discuss therapeutic decisions on an individual basis.[2]

Considerations Regarding Specific Pathogens and Antibiotics

Pathogens

The causative organism of infective endocarditis has significant impact on the course of disease, the occurrence of thromboembolic complications,[17,18] cardiac lesions,[19] and mortality[16,20,21] (table 1). The vast majority of cases are caused by Gram-positive cocci, *i.e.*, staphylococci, streptococci, and enterococci.[16,22,23] However, the microbiologic etiology of infective endocarditis shows significant variability due to regional differences and patient-related factors such as patient age, prevalence of rheumatic heart disease, prosthetic valves, cardiovascular implantable electronic device, or IV drug use.[22,27] Furthermore, the incidence of specific pathogens is changing over the years, with an increase of *Staphylococcus aureus* as the causative pathogen due to increasing healthcare-related infections,[24] or enterococci in the elderly patient.[28,29] Furthermore, the increased contribution of multiresistant pathogens such as methicillin-resistant *S. aureus* or vancomycin-resistant enterococci is a serious concern, as it necessitates treatment with second-choice antibiotics that are frequently less potent.[30,31] In about 10% of the cases, no causative microorganism can be found. Infective endocarditis caused by fungal infection or yeast, mostly found in patients with compromised immunity, is rare (about 2%) but associated with significant mortality.[1]

The majority of infective endocarditis–causing pathogens such as staphylococci, enterococci, and streptococci have the capability of forming complex biofilms resulting in increased

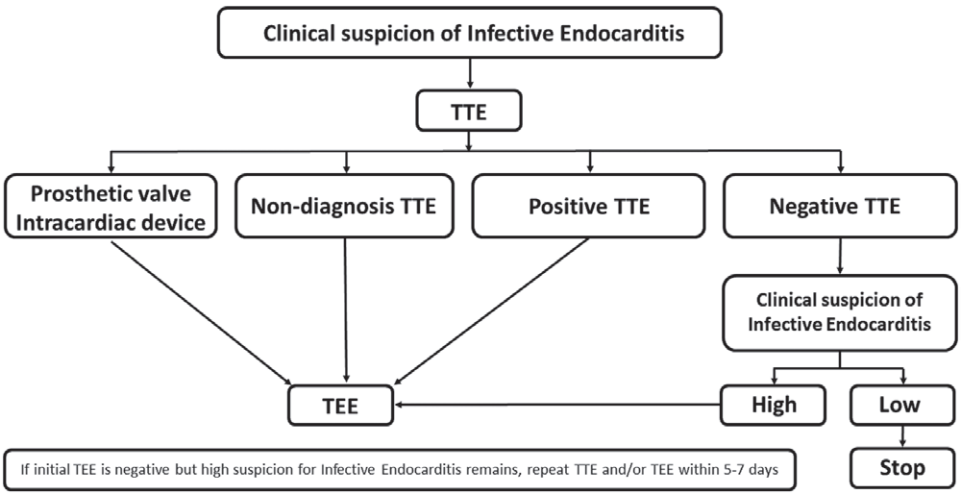

Fig. 2. Indications for echocardiography in suspected infective endocarditis.[9] TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

antibiotic tolerance and possibly poorer outcome.[32] The formation of biofilm in vegetations and on prosthetic materials is the reason endocarditis is treated with high doses of antibiotics over a long period of time. Given the difficulty of eradicating biofilm on prosthetic material in patients with infected cardiovascular implantable electronic devices, complete hardware removal is strongly recommended for these infections.[9,33] Prosthetic valve endocarditis without an indication for surgery can be effectively treated with antibiotics in a majority of cases.[34] Likewise, it is common practice to remove all indwelling intravascular catheters such as central venous lines or dialysis catheters before surgery, although no clear recommendations exist.

Antibiotics

Effective treatment of infective endocarditis consists of eradication of the pathogen by antimicrobial drugs supported by surgical treatment in selected patients. Generally, prolonged parenteral and bactericidal strategies are preferred. The specific antibiotic treatment should follow the available guidelines,[9,10] should adhere to local protocols, and might need to be adjusted to patient-related factors such as allergies and renal function. In many cases, initial therapy will be empiric and adjusted after identification of the pathogen.

Each antibiotic class displays specific pharmacologic properties regarding diffusion rate, distribution, and tissue penetration. Additionally, despite their potentially life-saving properties in infective endocarditis, antibiotics account for a relevant amount of adverse events.[35–37] The most common side effects and drug–drug interactions include nephrotoxic, hepatotoxic, and neurotoxic effects, direct interaction between antibiotics and the coagulation system,[38–41] anticoagulants such as warfarin,[42] or direct oral anticoagulants.[43] All of these interactions may increase the risk of bleeding complications. Table 2 shows an overview of the most relevant implications for the perioperative period.

Virtually all infective endocarditis patients are given IV antibiotics at the time of surgery. Whether additional antibiotic prophylaxis is necessary should be assessed on an individual basis. During surgery, not only impaired renal function but also the use of cardiopulmonary bypass (CPB) can significantly change the pharmacokinetic and pharmacodynamic properties of antibiotic agents. Hence, after initiation of CPB, plasma antibiotic concentration may fall below the required minimum inhibitory concentration for certain pathogens.[44] Furthermore, the use of intraoperative ultrafiltration can potentially decrease antibiotic serum levels.[45] In case of uncertainty on adequate dosing, an infectious diseases specialist and/or pharmacist should be consulted. Perioperative management of antibiotic therapy in infective endocarditis is thus still a field of uncertainties, in which further research is warranted.

Indication and Urgency of Surgery

Indications for surgery comprise heart failure, uncontrolled infection, and prevention of systemic embolic events. Here, heart failure is defined as a consequence of severe acute valve regurgitation, valve obstruction, or fistula. Uncontrolled infection is defined as infective endocarditis caused by particular virulent pathogens, such as fungal infection or involvement of multiresistant organisms, persisting positive blood cultures despite adequate antibiotic therapy, or the occurrence of local complications such as abscesses, false aneurysms, or fistulas. Prevention of embolization accounts for those patients who present with recurrent emboli and large, persistent, or enlarging

Table 1. Incidence and Association with Complication of Pathogens in Infective Endocarditis[3,10,16–26]

Cause of Endocarditis	Frequency	Mortality	Risk of Embolism	Cardiac Lesions	Changes in Incidence
S. aureus	~ 30%	+++	+++	+++	↗
Coagulase-negative staphylococci	~ 10%	+++	+	+++	↗
Viridans group streptococci	~ 20%	+	+	+	↘
S. gallolyticus (bovis)	~ 10%	+	+	+	↘
Enterococci	~ 10%	++	+	++	↗
Negative culture findings	~ 10%				→
Others	~ 10%				→
HACEK	~ 2%		++	++	
Fungi/yeast	~ 2%	+++	++		
Polymicrobial	~ 1%				
Coxiella	~ 1%				
Gram-negative bacillus	~ 3%			++	

+Risk abundant. ++Risk moderate. +++Risk high. ↗Increasing incidence. ↘Decreasing incidence. →Consistent incidence.
HACEK, *Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, *Kingella*.

vegetations.[9,10,13] While indications for surgery hardly differ between the available guidelines, the ideal timing for surgery is often less clearly defined. Mainly, the potential benefit of completion of antibiotic therapy before surgery has to be balanced against the risk of uncontrolled progression of infection with possible local or systemic complications.

The American Heart Association (Dallas, Texas)/American College of Cardiology (Washington, D.C.) guidelines generally recommend early surgical interventions for patients developing complications. Early surgery is defined in these guidelines as surgery during initial hospitalization and regardless of the completion of full antibiotic therapy.[10,13] The European Society of Cardiology (Brussels, Belgium) and Japanese Circulation Society (Tokyo, Japan) guidelines further differentiate into emergency surgery (performed within 24 h of diagnosis of infective endocarditis), urgent surgery (within a few days), and elective surgery (after completion of antibiotic therapy), and recommend urgent surgery for the majority of indications.[9,12] The American Association of Thoracic Surgeons (Beverly, Massachusetts) guideline recommends even more aggressive surgical treatment, stating that once surgical treatment is indicated, it should not be delayed at all, and patients should be operated within days.[11] Patients with one or more large mobile vegetations (greater than 10 mm in length) should

Table 2. Perioperatively Relevant Side Effects of Antibacterial Agents in Infective Endocarditis[35–37]

Antibiotic Class	Antibiotic Agent	Anaphylaxis	Renal	Hepatic	Neurologic	Hematologic*
Penicillins	Penicillin Ampicillin/amoxicillin Nafcillin/oxacillin/flucloxacillin	+++	++	+++	+	++
Cephalosporins	Cefazoline Ceftriaxone	+++	++	++		++
Carbapenems	Imipenem, meropenem	+++	++		+	++
Aminoglycosides	Gentamicin Streptomycin, netilmicin	+	+++		+++	+
Glycopeptides	Vancomycin Teicoplanin	+++	++			++
Rifamycins	Rifampicin	+	+	+++		++
Lipopeptides	Daptomycin					+
Oxazolidinones	Linezolide	+			++	+++
Tetracyclines	Doxycycline	+		++	++	
Quinolones	Ciprofloxacin, levofloxacin	+	++	++	+++	
Clindamycin	Clindamycin	+		++		+
Sulfonamides	Cotrimoxazole	++	++	++	+	++

+Risk abundant. ++Risk moderate. +++Risk high.
*Anemia, leukopenia, thrombocytopenia, coagulopathy.

even be operated immediately or within 48 h, due to the risk of (cerebral) embolization.[46]

There is currently a general trend toward earlier surgery in patients with infective endocarditis,[3,47] supported by evidence from a single randomized controlled trial,[48] several observational studies, and a meta-analysis that suggests early surgery is associated with lower mortality.[49] However, there is also evidence that surgery at a very early stage might not generally improve outcome.[50] This uncertainty illustrates the need to discuss timing of surgery in a multidisciplinary team.

If infective endocarditis is complicated by cerebrovascular events, timing is also controversial, mainly due to the risk of perioperative intracranial hemorrhage. However, evidence from retrospective single-center studies suggests that early surgery after embolic stroke is not associated with worse outcome.[51,52] One recent retrospective study even indicated that delaying surgery after embolic stroke increased the risk of neurologic and nonneurologic complications.[53] Accordingly, in the absence of severe neurologic damage such as coma, the respective guidelines recommend surgery to be considered without delay after stroke or subclinical cerebral embolization. However, in patients with major ischemic stroke and severe neurologic damage or intracranial hemorrhage, valve surgery should be delayed for at least 4 weeks.[9,10,13] Likewise, surgical treatment does not seem to improve outcome in infective endocarditis after transcatheter aortic valve replacement complicated by stroke.[54]

The persistent uncertainties about the optimal timing of surgery in infective endocarditis reflect the need for adequately designed clinical studies, ideally as a randomized controlled trial. However, to achieve a completed enrollment of the respective population of any meaningful study size is extremely challenging, which is also reflected by the scarcity of merely seven randomized controlled trials on infective endocarditis in the last 20 yr, most of which focused on antibiotic therapy.[3] Hence, evidence-based data are unlikely to be forthcoming in the near future, and an individual multidisciplinary risk–benefit analysis is utterly important, taking into account all medical and ethical considerations for immediately performing or delaying surgery.[55] In cases of extreme perioperative risk, multidisciplinary team discussion may result in advice against surgery even if it would be formally indicated.

Prediction of Outcome

The leading causes of death in infective endocarditis are heart failure, sepsis, cerebral embolism, and arrhythmias.[16] A number of risk factors predict outcome in infective endocarditis, especially when surgical treatment is indicated. Patient- and disease-related factors as well as infective endocarditis–mediated complications increasing the risk of mortality have been described[16,20,56–66] (table 3). The abundance of such risk factors may lead to poor prognosis, and due to the inability to withstand the surgical hit, this could be a reason to avoid surgery. This may be relevant for about 25% of patients with infective endocarditis.[67] Early surgery—when indicated—can decrease mortality.[48,49] Although some risk factors are similar in cardiac surgery for treating infective endocarditis compared to other surgical indications, there are several infective endocarditis–specific circumstances that are correlated to outcome.

Whether classical risk scores for adult cardiac surgery, *e.g.*, the European System for Cardiac Operative Risk Evaluation (EuroSCORE) risk model or the Society of Thoracic Surgeons score, are applicable to cardiac surgery for infective endocarditis is a matter of debate. Some studies showed a satisfactory risk stratification[68] while others demonstrated that the respective scores underestimated mortality in patients with infective endocarditis.[69] One reason for underestimation of risk may be the low prevalence of infective endocarditis in the cohorts used to develop the scores above (*e.g.*, 2.2% in EuroSCORE II [70]).

In order to estimate mortality risk in infective endocarditis more specifically, several infective endocarditis–specific risk scores have been developed (Supplemental Digital Content 1, http://links.lww.com/ALN/C777). It is currently unknown which score may serve best to predict mortality.[71–73] Many of these scores are generated on small numbers of patients from a single institution or region and are unlikely to perform well when moved into another treatment venue. Hence, it seems conceivable that local validation of infective endocarditis–specific scores can help to further improve the performance of scores. Calibration at our institution showed that EuroSCORE II was the most reliable risk score (unpublished data).

Echocardiography

Transthoracic echocardiography and transesophageal echocardiography (TEE) play a key role in assessment and management of infective endocarditis,[74] with a positive echocardiogram representing a major criterion according to the modified Duke criteria[14] (table 4). According to American Heart Association and European Society of Cardiology guidelines, transthoracic echocardiography is the first diagnostic test in a patient with clinical suspicion for infective endocarditis.[9,10] Of note, time to definitive diagnostic echocardiography is a significant predictor for infective endocarditis–related complications such as valve destruction, increased requirement for surgery and embolic events.[77]

Sensitivity and specificity in detecting vegetations on a native valve with transthoracic echocardiography are 60 to 70% and 90 to 94%, respectively; TEE has a much higher sensitivity (87 to 100%) and specificity (91 to 100%). Sensitivity in detecting a prosthetic valve vegetation with transthoracic echocardiography is 50%, compared to 85 to 95% with TEE.[9,74–77]

TEE should be performed in all patients suspected of prosthetic valve or intracardiac device infection. In addition, all patients with a positive transthoracic echocardiography,

Table 3. Factors Negatively Affecting Outcome in Infective Endocarditis

Patient-related Factors	Infective Endocarditis–related Factors	Complication-related Factors	Surgery-related Factors
Age	*S. aureus* infection	Cardiogenic shock	Urgent surgery
Female sex	Fungal infection	Septic shock	Previous cardiac surgery
Diabetes mellitus	Prosthetic valve infective endocarditis	Paravalvular complication	Cardiopulmonary bypass time
Comorbidity (immunosuppression, frailty, and others)	Nosocomial infective endocarditis	Stroke	Aortic cross clamp time
	Multivalve involvement vegetation > 10 mm	Renal failure	Re-sternotomy due to bleeding
		Persistent bacteremia	

or those patients with a negative or inconclusive transthoracic echocardiography but with high suspicion of infective endocarditis, should undergo TEE. When clinical suspicion remains high in combination with a negative TEE, a repeat echocardiography is performed within 5 to 7 days (fig. 2).[9,10] A practical piece of advice for general anesthesiologists is to invite cardiologists or cardiac anesthesiologists to perform TEE during or after noncardiac interventions in patients with suspected infective endocarditis under general anesthesia or deep sedation, thereby avoiding the need to undergo a separate anesthetic for the TEE.

A vegetation is typically characterized on echocardiography as an oscillating, irregularly shaped, heterogeneous intracardiac mass attached to endocardium or prosthetic material, mostly located on the low-pressure site of the affected valve. Identification of a vegetation may be difficult in the presence of preexisting valve lesions, in case of only small vegetations (less than 2 to 3 mm), or on a prosthetic valve. It can be challenging to differentiate infective vegetations from thrombi, Lambl's excrescences, cusp prolapse, papillary fibroelastoma, or fibrosis on device leads.[74]

Size and mobility of a vegetation are important echocardiographic predictors for new embolic events. A left-sided vegetation larger than 10 mm or a very mobile vegetation is at higher risk for embolization.[78] In case of a right-sided endocarditis, mortality is increased when the vegetation is larger than 20 mm.[79]

Table 4. Typical Echocardiographic Findings in Infective Endocarditis[9,10,53,75,77]

- Echocardiographic findings serving as major Duke criteria[14]
  - Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation
  - Abscess
  - New partial dehiscence of prosthetic valve
- Other echocardiographic features suggestive of endocarditis
  - New valvular regurgitation
  - New valvular perforation
  - Valve aneurysm
  - Nonspecific valvular thickening
  - Intracardiac fistulization

Periannular extension of infective endocarditis with abscess formation is a second hallmark of infective endocarditis on echocardiography. An abscess is a perivalvular cavity filled with necrosis and purulent material. A developing abscess may present as a region of periannular thickening. On echocardiography it shows as a nonhomogeneous echolucent, occasionally echodense area. By definition, there is no connection between the abscess and the adjacent blood pool. In case of pulsatile flow detection on color Doppler echocardiography, the abscess is frequently defined as a pseudoaneurysm. Sensitivity of transthoracic echocardiography and TEE in detecting an abscess is 50% and 90%, respectively.[9]

The third major echocardiographic criterion for diagnosing infective endocarditis is a new dehiscence of a prosthetic valve, which is characterized by paravalvular regurgitation and rocking motion of the valve prosthesis in cases in which more than 40% of the prosthetic valve annular area is dehiscent.[80]

Intraoperative echocardiography is recommended in all cases of infective endocarditis requiring surgery[13,74,81] (Supplemental Digital Content 2, http://links.lww.com/ALN/C795, shows a native aortic valve that is seriously damaged due to infective endocarditis with abscess cavity and pseudoaneurysm; Supplemental Digital Content 3, http://links.lww.com/ALN/C796, shows bioprosthesis endocarditis with a previously not identified fistula from aortic root toward the right ventricle). Inadequate preoperative testing or progression of disease can impact surgery. Hence, immediate intraoperative echocardiography before initiation of CPB was shown to change the operative plan in 11.5% of the patients.[82] Post-CPB TEE study is mandatory to guide de-airing, to aid weaning from CPB, and to evaluate surgical treatment, allowing a decision whether further surgical corrections are needed (in up to 10% of patients).[82]

While most echocardiography studies are done with two-dimensional TEE, three-dimenstional TEE may increase the accuracy of analysis of vegetation morphology as well as the prediction of the risk of embolization.[83,84] Future research will need to confirm the added value of three-dimensional echocardiography in the perioperative diagnosis and management of infective endocarditis.[85]

Coagulation, Bleeding and Transfusion in Patients with Infective Endocarditis

General Disease-related Alterations

Infective endocarditis goes along with a significant and complex interplay between inflammation and coagulation,[86] also called "immunothrombosis."[87] At various steps in the coagulation cascade, this interaction is involved in pathogenesis of infective endocarditis: upon activation of endothelial cells after the recognition of bacteria, a process vastly mediated by cytokines, tissue factor is released and activates the extrinsic coagulation pathway. In addition, coagulation factor XII is released and activates the intrinsic coagulation pathway. After activation of the coagulation cascade, prothrombin is cleaved to form thrombin, which in turn activates platelets and converts fibrinogen to fibrin.[6] It is noteworthy that platelets and fibrin form the main components of infective endocarditis lesions and hence valvular vegetations.

It has been suggested but not yet definitively proven that coagulation disorders, *e.g.*, inherited thrombophilia,[88] factor V Leiden, prothrombin G20201A mutation, or hyperhomocysteinemia, are associated with an increased risk for infective endocarditis.[89,90] Clinically, a hypercoagulable state may lead to maturation of endocarditis lesions and eventually thromboembolic events.[6] The risk of embolic events itself is associated with various coagulation laboratory parameters, *e.g.*, platelet factor 4[91] and mean platelet volume.[92]

In noncardiac surgery[93] and malignancies,[94] rotational thromboelastometry can predict thromboembolic complications, and it is conceivable that point of care coagulation testing may predict the risk of thromboembolic complications in patients with infective endocarditis. This, however, needs to be confirmed by future clinical studies.

Anticoagulation

During cardiac valve surgery using CPB, effective anticoagulation is mandatory, with heparinization followed by measurement of the activated clotting time (ACT) as standard for coagulation monitoring. Patients with infective endocarditis can present with relative heparin resistance,[95–97] which might even still be present after treatment with antibiotics for more than 4 weeks. Antithrombin III activity is lower and fibrinogen level higher in comparison to cardiac surgery patients without infective endocarditis.[98] Heparin resistance, in turn, is associated with hypercoagulable patterns in point of care coagulation testing,[99] and thus preoperative use of point of care coagulation testing might be able to predict heparin resistance in infective endocarditis, although this hypothesis requires confirmation. The treatment of heparin resistance comprises the administration of escalating doses of heparin (*e.g.*, in steps of additional 5,000 to 10,000 U), antithrombin (*e.g.*, 500 to 1,000 U), or fresh frozen plasma.[96,100,101] Whether one of those approaches is favorable in infective endocarditis–related heparin resistance is currently unknown. A recent survey by the Society of Cardiovascular Anesthesiologists (East Dundee, Illinois) revealed that 54% of the respondents used antithrombin concentrates as a first-line therapy.[101] Treatment algorithms to manage heparin resistance have been published and recommended use at the institutional level.[96,102] Moreover, there are reports on the use of alternative anticoagulation strategies such as bivalirudin[103] or nafamostat in patients with heparin resistance or infective endocarditis complicated by stroke, respectively.[104] Whether these form safe alternatives in infective endocarditis needs further clinical evaluation.

Bleeding and Transfusion

Whether the presence of infective endocarditis *per se* increases the risk of bleeding complications is currently not entirely clear. Normocytic–normochromic anemia is frequently present in infective endocarditis.[3] Although preoperative hypercoagulability is common in infective endocarditis, surgery may be cumbersome due to involvement of multiple valves and/or abscess formation, leading to long CPB time, which in itself is associated with increased need of blood transfusion, bleeding, and coagulation disorders.[105,106] Some studies showed an increased incidence of massive blood transfusion,[107,108] transfusion of platelets,[109,110] or postoperative active bleeding[111] in patients with infective endocarditis.

Management of coagulation in patients with infective endocarditis undergoing cardiac surgery is a two-edged sword. The risk of bleeding must be balanced against the risk of thrombotic complications in patients in a hypercoagulable state. In urgent or emergency procedures on patients receiving anticoagulants, *e.g.*, vitamin K antagonists or direct oral anticoagulants, management may even become more complex. In severe cases of infective endocarditis, hypercoagulability may turn into disseminated intravascular coagulation in the state of sepsis—increasing mortality and need for transfusion.[112]

In the bleeding cardiac surgical patient, perioperative treatment algorithms based on point of care coagulation testing are recommended to reduce the number of transfusions.[113] However, it is not known whether the normal values for non–infective endocarditis patients in existing treatment algorithms are equally useful in patients with infective endocarditis, and preliminary reports showed distinct patterns of hypercoagulability.[114]

Antifibrinolytic therapy is recommended in cardiac surgery and has been shown to reduce blood loss and transfusion rate,[113,115] despite data showing that tranexamic acid might be associated with increased risk of (cerebral) thrombotic events[116] and (at high dosage) a higher risk of postoperative seizures.[115] Patients with infective endocarditis show impaired fibrinolytic activity.[91,117] Thus, theoretically, the

risk of perioperative hyperfibrinolysis should be lower in patients with infective endocarditis.

Fibrinogen levels are elevated in infective endocarditis,[98] and although a certain decrease in fibrinogen concentration during cardiac surgery and CPB would be expected due to hemodilution[118] and bleeding/cell savage,[119] the need for fibrinogen suppletion should theoretically be lower in patients with infective endocarditis. However, meticulous monitoring of coagulation in the individual patient using classical laboratory values and/or point of care coagulation testing seems advisable.

Finally, specific pathogens, such as *S. aureus* or *Streptococcus gallolyticus*, might have a distinct effect on the coagulation system *via* kinases that activate prothrombin, plasminogen, or platelets as well as interaction with key coagulation proteins.[120,121] In addition, an interference of certain antibiotics with hemostasis and antithrombotic agents leading to significant bleeding complications has been described[122,123] (tables 4 and 5).

CPB

Effective anticoagulation is essential in cardiac surgery using CPB to prevent potentially devastating prothrombotic complications during extracorporeal circulation. Specific considerations concerning anticoagulation in patients with infective endocarditis are discussed in the "Anticoagulation" section.

Comparable to patients undergoing cardiac surgery for other reasons, prolonged CPB time (and aortic cross clamp time) in patients with infective endocarditis are associated with increased morbidity and mortality. In a retrospective study on 264 consecutive infective endocarditis patients, the prognostic cutoffs were found to be 166 min for CPB time and 72 min for aortic cross clamp time, respectively.[63] Not surprisingly, these cutoffs are lower than those seen in non–infective endocarditis patients.[125,126] These results suggest that patients with infective endocarditis might be more susceptible to the deleterious effects of prolonged CPB and aortic cross clamp times, arguably due to inflammatory cascades associated with infective endocarditis.

Mediators of inflammation can have detrimental effects on cardiac function.[127] During cardiac surgery for infective endocarditis, potential systemic spreading of bacterial lesions and use of CPB may lead to significantly increased cytokine levels and inflammatory mediators compared to non–infective endocarditis patients undergoing heart valve surgery.[128,129] Furthermore, certain cytokine profiles appear to be related to outcome in patients with infective endocarditis.[129,130] Some inflammatory biomarkers appear to be able to predict mortality in infective endocarditis, such as cytokines interleukin 15 and CCL4.[130]

There has been a debate on the effect of steroids on inflammatory response in cardiac surgical patients. The most recent analysis of the available literature states that the effect of steroids on mortality is uncertain, while the risk of myocardial injury might even be increased.[131] Ongoing research using thorough study protocols will need to clarify the potential benefits of steroids in cardiac surgery.[132] At this moment, however, the routine use of steroids in cardiac surgery is not recommended.[133] In patients with septic shock and ongoing requirement for vasopressor support, there is a weak recommendation for the use of corticosteroids according to the 2021 Surviving Sepsis Campaign Guidelines.[134] However, there is currently no available literature on the effect of perioperative steroids in patients undergoing cardiac surgery due to infective endocarditis, and thus additional studies are desirable in this particular patient collective.

A relatively new approach to hamper the inflammatory response in patients with infective endocarditis undergoing cardiac surgery is to remove inflammatory mediators by intra- or postoperative hemoadsorption. Here, blood purification with a cytokine adsorber is integrated into the CPB circuit. Preliminary clinical studies showed the feasibility and safety of perioperative hemoadsorption in patients with infective endocarditis[135,136] as well as a beneficial effect on the incidence of sepsis and hemodynamic stability.[137] Those

Table 5. Hemodynamic Goals for Common Infective Endocarditis–related Pathologies

Infective Endocarditis–associated Pathology	Heart Rate	Contractility	Preload	Afterload	Concerns
Aortic regurgitation	↑	n / ↑	↑	↓	Intra-aortic balloon counter pulsation contraindicated
Aortic stenosis	n / ↓	n / ↑	↑	↑	Maintain sinus rhythm CPR ineffective
Mitral regurgitation	↑	n / ↑	↑	↓	Avoid pulmonary hypertension
Mitral stenosis	↓	n	n / ↑	↑	Maintain sinus rhythm Avoid pulmonary hypertension
Tricuspid regurgitation	↑	n / ↑	↑	n / ↓	
Sepsis/septic cardiomyopathy	n / ↑	n / ↑	↑	↑	

n, Normal. ↑High. ↓Low. Adapted from Mittnacht *et al.*[124] Reprinted by permission of SAGE Publications.
CPR, cardiopulmonary resuscitation.

promising findings will have to be verified in randomized controlled trials such as the REMOVE trial.[138] Of note, while some cytokine absorbing devices have gained a European Conformity mark in Europe, in the United States, few devices only received U.S. Food and Drug Administration (Silver Spring, Maryland) Emergency Use Authorization for use in patients with severe COVID-19 and would not be available yet in patients with infective endocarditis.

Management of Organ Dysfunction

Cerebrovascular Disease

Cerebral complications are among the most feared and often devastating complications of infective endocarditis. The incidence of clinically relevant neurologic events is as high as 25%.[139] However, when silent cerebral complications are also taken into account, this incidence may reach 65 or even up to 80%.[140,141] The most common complications are ischemic stroke (about 70% of all neurologic complications) and intracranial or subarachnoid hemorrhage (15%), as well as meningitis (5%), brain abscess (5%), or infectious intracranial aneurysm (5%).[142] The main risk factors for neurologic complications are *S. aureus* infection, size of vegetations, mitral valve involvement, previous stroke, anemia, and nonneurologic embolic events.[78,139,143,144] Furthermore, high D-dimer levels were shown to be a strong predictor for ischemic stroke.[145]

Management of patients with infective endocarditis suffering cerebral complications comprises adequate antimicrobial therapy as early as possible and avoidance of anticoagulation. IV thrombolysis is generally not indicated, while in selected cases, endovascular treatment might be useful.[142,146–148]

When present, central nervous system complications represent a dilemma for the timing of surgery due to the possibility of hemorrhagic transformation as a consequence of intraoperative heparinization.[149] According to recent literature, early surgery seems to be safe in patients suffering from *ischemic* stroke. In patients with *hemorrhagic* stroke, surgery is advised to be delayed for 4 weeks.[150] Even in this high-risk population, however, early surgery might be feasible and lead to a favorable outcome; this decision is to be made by a multidisciplinary team on a case-by-case basis.[151]

Considering the intraoperative management of infective endocarditis patients with neurologic complications, there are no published data to support a specific anesthetic regimen or perfusion strategy, such as a predefined perfusion pressure during CPB.[152] Likewise, it is unknown whether intraoperative cerebral neuromonitoring, such as near-infrared spectrometry, processed electroencephalography, and others might be of any added value in this setting.[153] We strongly advise to meticulously document the preoperative neurologic status of the patient, and to reassess it postoperatively as early as possible.

In case of a new cerebral event detected postoperatively, therapeutic options are limited. In ischemic stroke, endovascular thrombectomy, possibly in combination with intra-arterial thrombolysis, might be an option in selected cases.[154] However, infective endocarditis carries a significantly worse outcome after mechanical thrombectomy compared to patients with other origins of ischemic stroke.[155] Neurosurgical intervention after cardiac surgery, *e.g.*, after new-onset intracranial hemorrhage, is accompanied by significant mortality. However, recent data suggest that neurosurgery *per se* does not seem to further increase mortality in this setting,[156] and again, a multidisciplinary case-by-case decision is to be made.

Circulatory Dysfunction

Acute heart failure in infective endocarditis is common, with incidences up to 40%,[157] and is an indication for urgent or emergency surgery.[9,10] Cardiac dysfunction can develop as a consequence of valve insufficiency due to perforation or destruction of valvular leaflets, as well as after rupture of the chordae tendineae or papillary muscle. Less frequently, large vegetations may cause valvular obstruction or aggravate preexisting valve stenosis. Furthermore, perivalvular abscess formation can lead to fistulas, perforations, and conduction block.[7] Here, the risk of periannular complications is higher in prosthetic than native valve infective endocarditis.[158] Acute coronary syndrome may occur as an embolic complication in 2% of patients with infective endocarditis, subsequently contributing to development of heart failure.[159] Finally, patients with infective endocarditis complicated by sepsis or septic shock can present particularly challenging hemodynamics, and septic shock will occur in up to 17% of patients with infective endocarditis during hospitalization.[160] The septic patient displaying vasoplegia and/or septic cardiomyopathy who also has heart failure due to valvular pathology is exceptionally difficult to manage; treatment will be on an individual basis.

Regarding hemodynamic management in patients with infective endocarditis, general physiologic considerations concerning preload, inotropy, and afterload in cardiac valve dysfunction apply (table 5).[124]

During CPB, patients with infective endocarditis are at increased risk for developing vasoplegia[161] as well as hyperlactatemia, which in turn is associated with post-bypass low cardiac output syndrome and increased morbidity.[162] Likewise, patients with infective endocarditis are generally at increased risk for postoperative hemodynamic instability. Besides duration of surgery, preoperative organ failure appears to be the most significant risk factor for high inotropic and vasoactive need postoperatively.[163] It is still unclear whether certain inotropes or vasopressors are superior to others in infective endocarditis. A small study in 42 patients demonstrated that a prophylactic single dose of methylene blue did not reduce vasopressor requirements or hemodynamic instability in cardiac surgical patients with infective endocarditis.[164] At this moment, the choice of drugs, *e.g.*, to treat vasoplegia, will rather be based on institutional protocols or expert consensus statements.[165]

The overall incidence of new-onset atrial fibrillation in infective endocarditis is 8 to 10%, and new-onset atrial fibrillation serves as a strong predictor for heart failure and mortality.[166,167] The general incidence of postoperative atrial fibrillation after cardiac surgery is 20 to 40%[168] while the exact incidence of postoperative new-onset atrial fibrillation in surgically treated infective endocarditis is yet unknown.

In case of circulatory failure resistant to pharmacologic intervention, temporary mechanical support is an option. However, in patients with infective endocarditis undergoing veno-arterial extracorporeal membrane oxygenation, the outcome seems to be poor, although evidence is sparse.[169,170]

The presence of preoperative heart failure and consecutive need for cardiovascular or respiratory support significantly affect outcome in patients with infective endocarditis.[171] However, patients in cardiogenic shock still show a superior outcome after cardiac surgery compared to patients in septic shock undergoing surgery.[58]

Renal Dysfunction

Acute renal failure or acute kidney injury complicates up to 30% of all cases of infective endocarditis and is associated with a significantly worse prognosis.[16,172] Likewise, patients with chronic renal failure who are undergoing hemodialysis show very poor outcomes in case of infective endocarditis.[173] Consequently, renal failure is part of several scoring systems for prediction of outcomes in infective endocarditis.[59,174–176]

Several mechanisms are responsible for the development of acute renal failure in infective endocarditis. Infection-related immune complex–mediated glomerulonephritis is the most common and is seen in more than 80% of acute kidney injury cases in infective endocarditis.[177] Embolic renal infarction and renal cortical necrosis are other causes. Finally, acute kidney injury can be a complication of antibiotic therapy (table 5): penicillins, cephalosporins, and quinolones can lead to acute interstitial nephritis, whereas aminoglycosides are associated with acute tubular necrosis. The exact mechanism of vancomycin nephrotoxicity is unclear, but renal tubular ischemia due to oxidative stress has been postulated, as well as a cast nephropathy.[178]

The treatment of infective endocarditis–associated acute renal failure focuses mainly on antibiotics and cardiac surgery as indicated for the underlying infection, avoidance of nephrotoxic drugs, and supportive therapy. In the case of infective endocarditis–associated glomerulonephritis, immunosuppressive therapy in addition to antibiotics has been administered, although the evidence rests on case reports and expert opinion.[177] Another specific renal protective approach, the perioperative administration of sodium bicarbonate, has not been proven to be effective in patients with infective endocarditis.[179]

Pulmonary Complications

Pulmonary complications are predominantly associated with right-sided endocarditis and can occur in up to 50% of those patients.[158] Risk factors for the development of right-sided endocarditis are IV drug use, the presence of cardiovascular implantable electronic devices or central venous catheters, and congenital heart disease with right-sided abnormalities.[180,181] Apart from the last, the global incidence of these risk factors is increasing, and consequently, right-sided infective endocarditis is becoming more common.[181]

Septic embolization into the pulmonary vasculature can lead to pulmonary infarction, pneumonia, pulmonary abscess formation, pleural effusions, empyema, and pneumothorax.[181] The removal of offending implanted devices is obviously indicated, and after that, right-sided infective endocarditis usually responds to medical therapy, making cardiac surgery less frequently necessary compared to left-sided infective endocarditis.[181] The treatment of the pulmonary complications themselves is mostly conservative, and prompt and marked improvement of pulmonary abnormalities on imaging after antibiotics and cardiac surgery has been described.[182]

Liver Dysfunction and Splenic Complications

Preexisting liver disease predisposes to infective endocarditis[183] and influences prognosis and mortality: particularly liver cirrhosis is much more prevalent in nonsurvivors of infective endocarditis.[60,184] However, a large cohort study showed that the *degree* of preexisting liver disease has important prognostic consequences: patients with Child Pugh A liver cirrhosis had comparable outcomes to noncirrhotic patients, both with surgical and conservative treatment. Only in stages B and C was the outcome significantly worse. The authors therefore advocate to treat Child Pugh A patients as aggressively as patients without chronic liver disease.[185]

Compared to preexisting liver disease, little can be found in the literature about *de novo* liver dysfunction as a complication of infective endocarditis. In a retrospective single-center analysis of 285 patients with infective endocarditis but without preexisting liver disease, referred for cardiac surgery, pre- as well as postoperative liver dysfunction significantly increased mortality (up to 50% in-hospital). The most common mechanism was hypoxic hepatitis, which in itself has a poor prognosis. The duration of operation and CPB time were described as risk factors for developing hypoxic hepatitis.[186]

There is no specific treatment for hepatic failure in infective endocarditis; treatment principles follow the general lines of supportive therapy. Liver dysfunction commonly leads to coagulopathy, which increases the risk for perioperative bleeding and requires aggressive therapeutic correction.

Finally, splenic infarcts and abscesses need to be mentioned. Abscesses are relatively common (up to 5%) and relevant because they constitute an extracardiac septic focus that can sustain systemic infection. Multiple splenic abscesses or an abscess not amenable to percutaneous drainage are indications for splenectomy. The sanitation of the septic focus is, if possible, performed before cardiac surgery.[158,187] More aggressive and advanced imaging in recent years shows that abdominal involvement in infective endocarditis is more common than

previously thought. Magnetic resonance imaging revealed abnormalities in spleen, liver, or kidneys in 34% of patients.[188] Consequently, according to the 2015 European Society of Cardiology guidelines, imaging-derived evidence of vascular phenomena alone is now judged to fulfill this minor Duke criterion, even in the absence of clinical findings.[9]

Postoperative Care

Virtually all surgically treated patients with infective endocarditis will be admitted to the intensive care unit postoperatively. Here, the management of organ dysfunction is the predominant challenge, especially within the first 24 h after cardiac surgery[189] (see the "Management of Organ Dysfunction" section). The most common postoperative complications are persistent septic shock, refractory heart failure, coagulopathy, acute renal failure, stroke, and conduction abnormalities.[190] While cardiac valve dysfunction should be fixed after cardiac surgery, myocardial ischemia or stunning might lead to poor contractility, eventually leading to refractory heart failure. Furthermore, septic shock, accompanied by vasoplegia and/or septic cardiomyopathy, can still develop or aggravate after surgery.[160]

Postoperative bleeding complications are frequent after cardiac surgery for infective endocarditis, due to either surgical bleeding or coagulopathy. The latter may originate from several factors such as hemodilution, hypothermia, sepsis, and the use of CPB. Beside the need for resternotomy, postoperative coagulopathy might also increase the risk for intracranial hemorrhage.[191] Meticulous postoperative coagulation management is thus crucial in patients with infective endocarditis.

In case of local extension of infection to paravalvular tissue, the cardiac conduction system can be damaged, either by the infection itself or due to surgical trauma. Hence, postoperative atrioventricular block requiring a permanent pacemaker can occur. This complication is seen in about 13% of patients undergoing cardiac surgery due to infective endocarditis. Given the increased risk of reinfection in patients with infective endocarditis, the timing of permanent pacemaker placement should be carefully evaluated by an interdisciplinary team.[192]

The continuation of antibiotic therapy leading to adequate plasma levels is crucial in order to reduce the risk of prosthetic valve endocarditis. Here, dosing might need to be adjusted according to organ dysfunction and/or mechanical organ supporting therapy.

Finally, patients with infective endocarditis are at lifelong increased risk for reinfection. Hence, accurate follow-up, also after discharge from the intensive care unit and from the hospital, is essential to prevent readmission and reinfection, *e.g.*, in the form of treatment of opioid use disorder in patients with IV drug use.[193] Furthermore, patients with successfully treated infective endocarditis are recommended to receive antibiotic prophylaxis when they undergo procedures that are accompanied by bacteremia.[13]

Future Directions

Changes in Epidemiology

The past decades have seen a steady increase in the incidence of infective endocarditis,[3,194] especially in the elderly.[21] This trend is probably related to several factors: an aging population in general with a higher life expectancy also among patients with congenital heart defects, and an expanding number of cardiovascular implantable electronic devices and prosthetic valves. Of note, prosthetic valve endocarditis by now accounts for 30% of all cases of infective endocarditis and has the worst outcome.[16] Likewise, infective endocarditis is currently health care–associated in more than 25% of the cases.[23] Accordingly, the microbiologic profile is changing, with infective endocarditis caused by staphylococci and enterococci on the rise.[16,21]

Nowadays, elderly and frail patients can successfully be treated using less invasive valve interventions, such as transcatheter aortic valve replacement or percutaneous mitral or tricuspid valve repair, with reduced procedural risks and faster recovery.

Patients suffering from infective endocarditis after a transcatheter aortic valve replacement procedure represent a particular challenge due to frailty and multimorbidity. In many cases, open heart surgery has previously been rejected. Generally, the incidence of infective endocarditis after transcatheter aortic valve replacement varies between 0.4 and 3.1% in the first year, which is not significantly different from the incidence after surgical aortic valve replacement.[195] In transcatheter aortic valve replacement patients, infective endocarditis is predominantly caused by staphylococci and enterococci.[196] Interestingly, the risk of infective endocarditis after transcatheter aortic valve replacement seems to be increased after treatment in a catheterization laboratory when compared to a hybrid operating room.[197,198]

Although the outcome after conservative treatment is very poor (1-year mortality of up to 75%), open heart surgery after transcatheter aortic valve replacement carries extremely high risk, while transcatheter valve-in-valve treatment might be feasible in exceptional cases.[3] These challenges explain why only about 15% of patients with infective endocarditis after transcatheter aortic valve replacement are treated surgically compared to 50% of other patients with prosthetic valve endocarditis.[199]

Another important and also growing group is IV drug users presenting with infective endocarditis. The significant increase in the past 10 to 15 yr, particularly in the United States, is related to the current opioid crisis. With considerable regional variability, IV drug users now represent up to 30% of all surgically treated cases of infective endocarditis in the United States.[200] IV drug users form a unique patient group within cardiac surgery. Patients are more likely to be young, be male, have low socioeconomic status, have fewer comorbidities, and have human immunodeficiency virus infection, hepatitis C, concomitant alcohol abuse, and

liver disease. Likewise, the prevalence of mental illness and homelessness is increased.[193,201]

Due to their lower cardiopulmonary risk, 30-day mortality is lower in this specific patient population than in non–IV drug users with infective endocarditis, but long-term outcome is often compromised by recidivism and reinfection.[202] IV drug use is associated with a fourfold risk of reinfection,[203] and recidivism is the leading cause of death.[204] Nevertheless, the question of whether surgical intervention should be performed remains an individualized decision in which healthcare costs and ethical and legal arguments should be weighed.[205] Postoperative follow-up and comprehensive health care, with special emphasis on treatment for opioid use disorder, may reduce the risk of reinfection and mortality in IV drug use.[193]

Surgical Advances

Comprehensive guidelines concerning surgery for infective endocarditis are available.[9,10,46] Remarkably, only about 10% of the recommendations in these guidelines are based on level A evidence.[47,206]

The cornerstone of surgical treatment in infective endocarditis is the removal of all infected and necrotic tissue, as well as removal of foreign material with consecutive reconstruction of cardiac morphology.[9,11] In native valve endocarditis, valve repair is performed whenever possible, provided that infection is limited to cusps or leaflets.[46,207] Repair should be attempted, particularly with infective endocarditis of the atrioventricular valve, and may occasionally be possible with infective endocarditis of the aortic valve. In case of prosthetic valve endocarditis or advanced valve destruction, valve replacement is most likely indicated. Regarding the type of valve, a recent meta-analysis showed no significant difference in overall survival or rate of valve reinfection between patients treated with mechanical valves and patients treated with bioprosthetic valves.[208] The choice of mechanical or biologic prosthesis should hence be based on the patient's age, life expectancy, comorbidities, expected compliance concerning anticoagulants, and patient preferences. In case of intracranial bleeding or major stroke, however, mechanical valves should be avoided to reduce necessity of postsurgical anticoagulation therapy. When aortic valve infective endocarditis extends to the aortic annulus and/or the aortic root, an allograft or stentless xenograft may be beneficial.[46,209,210] Sutureless valves might represent an option for selected high-risk patients, but further research is still needed.[211] In case of extended left-sided infective endocarditis, double valve replacement or even extended reconstruction of the mitral-aortic intervalvular fibrosa or additional surrounding tissue may be necessary—a procedure accompanied by high mortality, sometimes described as a "commando procedure."[212] In very exceptional cases, heart transplantation might be the last option to treat infective endocarditis.[213]

In general, sternotomy is the preferred access.[46] However, in isolated atrioventricular valve endocarditis, minimally invasive surgery might be suitable in specialized centers,[214] with the respective implications for anesthesia management. Yet TEE must have excluded the involvement of nonatrioventricular valves and surrounding structures.

Treatment paradigms beyond classical valve repair or replacement are currently not standard of care. In IV drug users presenting with tricuspid valve infective endocarditis, removal of the tricuspid valve leaflets and chordae tendineae without replacement, hence valvectomy, might represent an acceptable initial approach.[215] Likewise, for IV drug users with infective endocarditis, percutaneous debulking of large tricuspid valve vegetations by mechanical aspiration might serve as treatment or a bridging strategy to definitive surgery.[216,217] Transcatheter aortic valve replacement is generally contraindicated in the context of endocarditis; however, it may still serve as a feasible option in exceptional or emergency cases.[218]

There is a noticeable trend to be therapeutically more aggressive in patients with imminent risk of embolism[46] and increasing age. This increase in the number of high-risk patients will present cardiac surgeons and anesthesiologists with a challenge, especially in terms of decision-making. Around 25% of patients with an indication for surgery are already not operated on[67]—a number that is likely to increase in the future.

Endocarditis Team

A multidisciplinary approach is now considered mandatory in the management of infective endocarditis,[219] as adequate treatment inevitably requires the expertise of various medical specialists. This is also reflected in the recommendations of the current guidelines advocating an endocarditis team to treat patients with infective endocarditis.[9,10,13] Several studies using a before–after design showed that the introduction of a multidisciplinary endocarditis team improves outcome in patients with infective endocarditis.[220–223]

Permanent members of endocarditis teams are inherently cardiologists, infectious disease specialists, microbiologists, and cardiac surgeons, supplemented on indication by imaging specialists, congenital heart specialists, and electrophysiologists.[9,13] At least for surgically treated patients, both cardiac anesthesiologists and intensivists with experience in the treatment of cardiac surgery patients should join the team.[224] Furthermore, neurologists, interventional neuroradiologists, geriatricians, addictionists, or other specialists are involved in special circumstances.[13]

Beside clinical management of infective endocarditis patients, endocarditis teams ideally are also involved in patient and nonspecialist education, participation in data registries, and research activities.[9,219,224] In a recent survey across 100 European centers, two thirds of all institutions has installed a specific endocarditis team to support decision-making.[225] Where this has not yet been established, it should strongly be recommended to build up an endocarditis team—a team in which, we believe, cardiac anesthesiologists

Table 6. Recommendations to the Anesthesiologist Caring for Patients with Infective Endocarditis

- Become a structural member of the multidisciplinary endocarditis team
- Get involved in preoperative risk assessment and decision-making
- Study preoperative imaging, perform thorough intraoperative echocardiography (focus on possible progress of disease); if in doubt, consult imaging specialist
- Continue preoperative anti-infective therapy at adequate dose, conceivably adjusted for organ dysfunction or cardiopulmonary bypass; if in doubt, consult infectious disease specialist and/or pharmacist
- Prepare for coagulation abnormalities including heparin resistance and possibly increased risk of bleeding, use point of care coagulation testing
- Prepare for prolonged cardiopulmonary bypass and aortic cross clamp times, with possibly increased risk for myocardial dysfunction and vasoplegia

can be of extraordinary added value due to their expertise in the perioperative management of critically ill patients.

Conclusions

Our review offers anesthesiologists who care for patients with infective endocarditis a summary of the most important disease-specific features in the perioperative care of this high-risk patient group. In addition, our literature research reveals the lack of scientific data about treatment of patients with infective endocarditis from the perioperative phase. Therefore, we strongly encourage further clinical research to optimize the treatment of these patients.

The medical treatment of infective endocarditis invariably warrants a multidisciplinary approach. Since around half of all hospitalized patients with infective endocarditis have to be operated on, an early discussion in a multidisciplinary perioperative team, which also includes anesthesiologists and intensive care specialists, appears to be indispensable. Table 6 shows recommendations to the anesthesiologist caring for patients with infective endocarditis.

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