Chapter

# Endocarditis: Cardiac Surgery Treatment/A Thrilling Challenge in Cardiac Surgery

*Dario Buioni, Paolo Nardi, Claudia Altieri, Calogera Pisano and Giovanni Ruvolo*

## Abstract

Infective endocarditis is a rare but life-threatening disease that has a major impact on healthcare resources. It is heterogeneous in etiology, clinical manifestations, and course. The timing of surgery remains a topic of debate. Some authors promote an early surgical approach to improve the outcomes. There are different points of view between American and European guidelines regarding the relative priority of surgery over medical treatment. Anyway, multidisciplinary teams and multimodality strategies are advocated in order to optimize the treatment according to the individual needs of the patients. The early surgical approach may represent a valuable treatment option for high-risk patients. In this chapter, we discuss the latest evidence on surgical approaches, potential pitfalls, and the controversial issues in the contemporary practice of infective endocarditis.

**Keywords:** complicated infective endocariditis, cardiac device, surgical recostruiction, echocardiography imaging, prosthetic heart valve

## 1. Introduction

Infective endocarditis (IE) is a rare but severe cause of sepsis that consumes considerable healthcare resources and requires multidisciplinary approach. It affects 3–10 per 100,000 per year in the population, and the incidence seems to be slightly increasing [1]. Therefore, up to 40–50% of affected patients require valve surgery during the clinical course, with overall mortality remaining around 20–25% per year in most published series. First described by Lazare Riviere in the seventeenth century, but William Osler better characterized the clinical manifestations [2]. Given its complexity, the management of infective endocarditis requires the close collaboration of multidisciplinary approach, Endocarditis Team, mandatory for the appropriate initial treatment. It is generally agreed that those decisions on both the indication and timing of surgical intervention should be determined by multi-specialists with expertise in cardiology, imaging, cardiac surgery, infectious disease, and neurology [3]. Approximately 50% of patients will require early surgery, but there are concerns that performing the procedure during an active infection, before the valve is completely sterilized, may lead to an increase in post-operative complications. Despite the rapid diagnosis and early intervention, 1-year

mortality associated with erectile dysfunction has not improved in recent decades. Infectious endocarditis on prosthetic material after percutaneous procedures represent over 25% of all cases and include electronic implantable cardiac device (CIED), TAVR transcatheter aortic valve replacement, non-electronic devices (percutaneous occluder), cases of which are on the rise and create unique clinical challenges [4]. Interventions are characterized by a high risk of mortality. The use of surgery has gained a phase in the treatment of IE, and it is expanding. Current guidelines are cautious in board indication of surgery in aggressive left-sided endocarditis [5]. Early surgery is highly recommended in patients with IE with signs of congestive heart failure, while surgery to prevent systemic embolism remains debated. Indeed, main concern for patients with large vegetation high-risk embolism [6]. In these cases, the early surgery approach with complete excision of infected tissue and valve repair has been achieved in high-volume centers with low mortality, suggesting the benefit of early surgical management [7]. Concerns remain regarding the technical challenge of surgery in the active infection and inflammatory responses. The 2015 American College of Cardiology-American Heart Association (ACC-AHA) and European Society of Cardiology guidelines on the use of early surgery have different approaches and non-univocal recommendation [8]. There is a difference in the assessment of endocarditis between the European and American guidelines that can guide the decision-making aspect. For the ESC guidelines, distinguish emergency surgery (performed within 24 h), urgent surgery (within a few days), and elective surgery (after 1–2 weeks of antibiotic therapy), with an urgent basis for the majority of cases [9–11]. AHA guidelines define early surgery as during initial hospitalization and before completion of a full course of antibiotics. At the moment, there are no randomized studies that can help us reach the best conditions for the surgery and, therefore, the right times. Crucial for the best surgical outcome, to perform it at the right time, especially in patients with prosthetic valve endocarditis, which occurs in 3–6% of patients within 5 years of surgery and is characterized by high morbidity and mortality. Many patients considered at intermediate to high risk or inoperable that have undergone TAVR are also susceptible to IE on these prostheses [12, 13]. There are well-known patients subset that are at higher risk due to anatomical features of valve heart disease and coexistent comorbidities, with more than 10% of patients considered to be at too high risk for surgery [14].

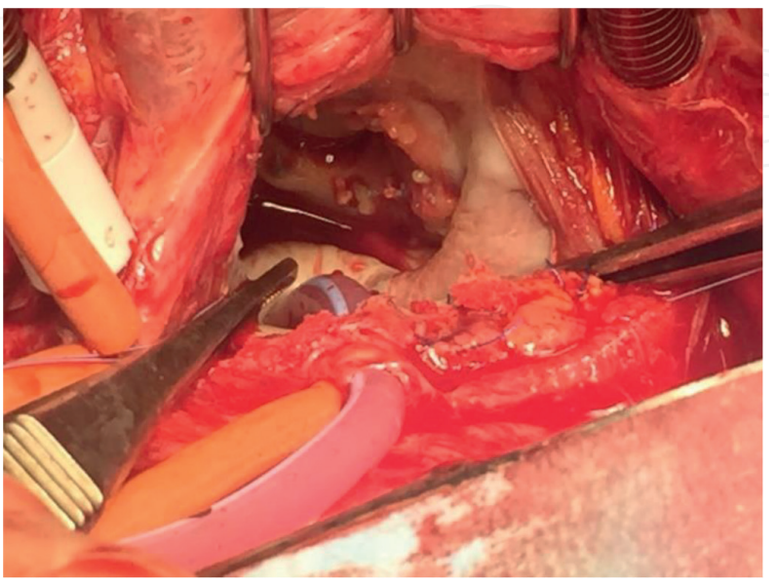

**Figure 1.**
*Mitral annulus endocarditis.*

Although surgical techniques, prosthetic models, anesthesiology, and infectiology approaches have constantly improved over the last years, increased higher-risk cases may affect operative success, in terms of higher mortality. Finally, surgery approach; valve conservation is especially important in less developed populations where compliance with medical therapy, especially anticoagulation, is poor, and bioprostheses are prone to early degeneration in young patients. Repair of the aortic valve is generally only applied to minor lesions, such as localized perforations of the cusps and vegetations that do not significantly alter the valve structure. In contrast, there is a wider scope for conservation of the mitral valve (MV); several studies have confirmed the feasibility of MV repair in the healed and active phase of IE and have shown better long-term results in comparison with valve replacement. Several authors used a minimally invasive or endoscopic approach. In this chapter, we will discuss the surgeon's point of view and can be given answers regarding the best strategy to be adopted in the early treatment of IE (**Figure 1**).

## 2. Epidemiology

In the past, rheumatic heart disease was a predisposing condition, but is nowadays less commonly detected among cases of infective endocarditis, although the importance of such predisposing conditions persists in low-income countries [15]. Therefore to know the real patient age, comorbidities, place of acquisition, type of endocarditis, microbiological data, and mortality rate worldwide. Cases associated with intravenous drug use have decreased, but dramatic increase in North America and in some Eastern European countries [16]. In high-income countries, cases are increasing for degenerative valve disease, intracardiac devices, indwelling catheters, and immunosuppression [17, 18]. This explains why the latest analyses of the demographic of endocarditis cases show a trend toward nosocomial characteristics, elderly patients, staphylococcal, enterococcal cases, and the involvement of prosthetic valves and cardiovascular implantable electronic devices (CIEDs). Other etiologies: 2–5% can be produced by Gram-negative bacilli (HACEK group [19]). Fungal endocarditis accounts for less than 2% of cases, mainly caused by yeasts of the genus *Candida spp* and rarely by other filamentous fungal yeasts [20]. A variable proportion (up to 10–20% of cases) without documented etiology is considered "culture-negative endocarditis" mostly as a consequence of prior administration of antibiotics or caused either by slow-growing microorganisms or from intracellular bacteria that are difficult to cultivate (e.g., *Chlamydophila spp*., *Bartonella spp*., *Tropheryma whipplei*). *Staphylococcus aureus* is the most frequently isolated pathogen in high-income countries with a reported percentage of 30% of cases. Habib et al. In the EURO-ENDO registry, from 1 January 2016 to 31 March 2018, centers were asked to include consecutive patients aged greater than 18 years who presented with IE during a 1-year period [21]. A total of 156 centers from 40 countries included 3116 cases of IE, representing an average of 20.19 patients per center per year offers a unique opportunity to assess the current characteristics of IE in Europe [22]. It allows us to consider clinical presentation, microbiology, complications, management, and prognosis. Several countries outside Europe also participated in this study, allowing the analysis of IE on the basis of geographical and socioeconomic factors. It will allow a comparison with the EuroHeart survey [23, 24]. The main messages emerging from EURO ENDO: IE most frequently affects men around 60 years of age; prosthetic valve infective endocarditis (PVIE), CIED, nosocomial, staphylococcal, and enterococcal endocarditis are more frequent. Sepsis and septic shock are severe complications that may arise from any type of infection, which can eventually lead to a multiorgan failure. It appears to be

associated with particularly virulent microorganisms such as *S. aureus* and beta-hemolytic Streptococci. Indeed, due to their invasive and destructive effects on the affected anatomical structures, these bacteria can seed distant septic metastases. The extraction of exotoxins that can act as superantigens, which overactivate the immune system. The systemic inflammation that is consequently triggered has an important hemodynamic impact, with endothelial dysfunction and a drop in vascular resistance. This serious situation explains why the presence of septic shock is associated with an increase in the risk of mortality. IE develops in three stages: bacteremia, adhesion, and colonization. In bacteremia, bacteria enter the bloodstream via the mouth, gastrointestinal, and urinary tracts, or the skin, through venous catheters or after an invasive medical or surgical procedure. Adhesion: whereas the normal endothelial lining of the heart is resistant to bacterial adhesion, bacteria are able to adhere to abnormal or damaged endothelium via surface adhesins. These proteins mediate attachment to extracellular host matrix proteins, facilitated by fibrin and platelet microthrombi. Bacterial adhesion gives rise to colonization; cycles of bacterial proliferation occur in addition to thrombosis, monocyte recruitment, and inflammation, leading to formation of mature vegetation. Many of the microorganisms produce biofilms that protect bacteria host immune defenses, impede antimicrobial efficacy, and hide resistant persister organisms. Biofilm is an important determinant of virulence in staphylococcal device-related infections. In general, three blood culture series detect the presence of pathogens in 96–98% of bacteremia who have not yet started antibiotic therapy, in coagulase-negative Staphylococci. The blood culture does not need to be done at the febrile peak because the presence of the pathogen is not related to the extent of the fever. It's possible that no pathogen growth from blood cultures delays diagnosis, which, is reported in up to 10% of cases. Fungal endocarditis usually caused by Candida or Aspergillus, is very aggressive and often fatal because it occurs in the immunosuppressed patient or after cardiac surgery, mainly in prosthetic valve recipients. After surgery can help in the microbiological diagnosis through the use

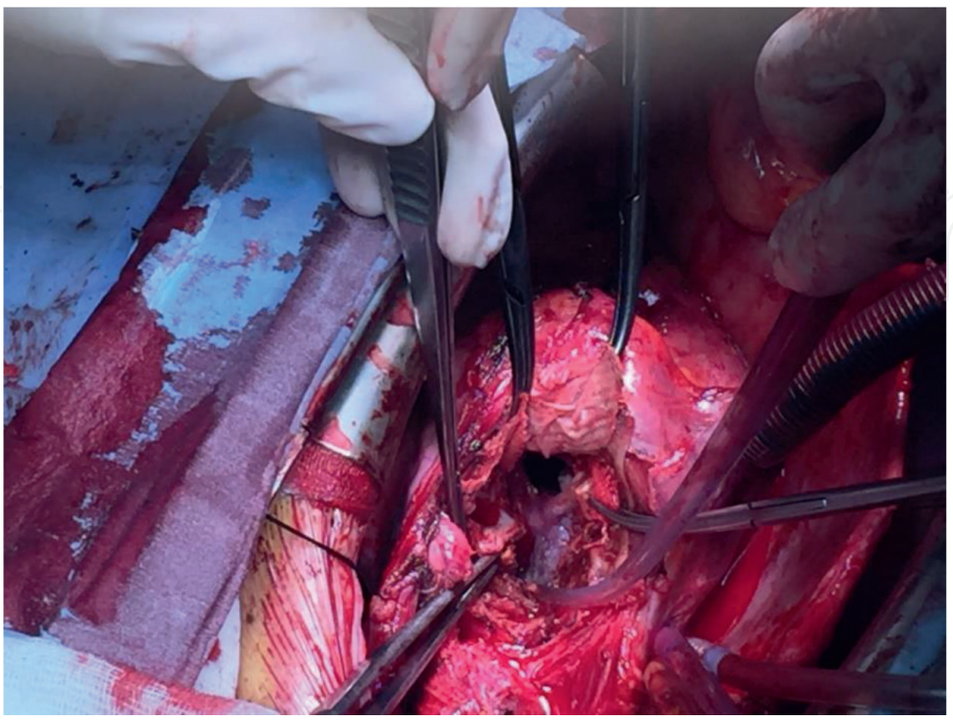

**Figure 2.**
*Prosthesis aortic valve infection.*

of complementary molecular techniques such as a polymerase chain reaction for pathogen DNA (PCR). Particularly useful in patients that received antibiotics, as bacterial DNA often persists even for non-cultivable pathogens (e.g. *T. whipplei*). PCR often carries the risk of false positive results due to contamination of the sample. New techniques combining PCR and mass spectrometry promise direct characterization of bacteria in peripheral blood or valvular tissue. The infection that occurs on cardiac devices is sustained by reactive inflammatory and thrombotic phenomena (**Figure 2**).

## 3. Diagnosis

The diagnosis of IE is based on clinical, microbiological, and imaging data, as specified by the modified Duke criteria. Clinical features of infective endocarditis remains a critical feature in diagnosis, primarily for subacute and chronic forms. For diagnosis the information proposed by blood cultures, and different imaging can accurately define anatomical aspects such as vegetation or other complications [25].

## 4. Imaging

Transthoracic echocardiography (TTE) is the main method in the diagnosis of endocarditis; remains cornerstone of imaging and is rapid, straightforward, and may diagnostic. TTE is the recommended initial modality of choice for both native or prosthetic valve infective endocarditis (TTE) varying sensitivity rates for valvular and paravalvular abnormalities such as vegetations, new regurgitation, or dehiscence of a prosthetic valve perforations, abscesses, and fistulae. Transesophageal echocardiography TEE is indicated when TTE is positive or nondiagnostic, when complications are suspected, or when intracardiac device leads are present. This technique can also differentiate vegetations from thrombi and can be used in surgical planning. A growing interest in the use of cardiac computed tomography (CT) [26]. CT shows anatomical correlation, especially when diagnosing a perivalvular abscess of the aortomitral intervalvular fibrous body and structures surrounding the aortic root. Cardiac CT is frequently used to preoperatively assess the presence of coronary artery disease in aortic endocarditis where performing a coronary angiography carries a prohibitively high risk of dislodging of vegetation. In early diagnosis, excellent results are obtained in measuring biological activity by emission of 18 F-fluorodeoxyglucose positron/computed tomography (FDG-PET/CT) and CT/CT with emission of single photons of radiolabelled white blood cells (WBC-SPECT/CT). These investigation methods have been recommended by the European Society of Cardiology in patients with suspected endocarditis on valves implanted for more than 3 months, whose positive value has been included as the main criterion for the diagnosis of the germ and therefore of device-related endocarditis [27]. Several studies on patients with suspected PVE have demonstrated an important diagnostic value of FDG-PET/CT and WBC-SPECT/CT and suggest that two imaging techniques can be used in a stepwise fashion when evaluating the presence of endocarditis. FDG-PET/CT should be used first, for higher sensitivity and if the results are not conclusive, WBC-SPECT/CT may be performed. Controversy remains on the use in patients with aortic root grafts with a prosthetic valve, since a high rate of false positives. In the diagnosis of NVE, the role of FDG-PET/CT has not been fully established and may be limited when endocarditis is strongly suspected but the DUKE criteria are not met [28]. Brain CT is often used when

neurological symptoms are present, and magnetic resonance imaging (MRI) has better sensitivity in defining lesions. Routine cerebral RMI identifies abnormalities in 80% of patients. Routine cross-sectional imaging of the brain, chest, spine, spleen, liver, and kidneys has not demonstrated a clear utility, but evidence of embolism by cross-sectional imaging is a novel minor diagnostic criterion in the ESC 2015 guidelines.

## 5. Surgery approach

The objectives of surgery are as follows: remove possible sources of embolism; remove both infected tissue and foreign material; restore cardiac integrity, close any cavities; and often restore both the aortic mitral junction and the left ventricular outflow tract. Many surgical techniques have been used or invented both full sternotomy and minimally invasive approaches, but a clear long-term advantage of one technique has yet to be proven [14, 29, 30]. Surgery is currently performed in 50–60% of patients, and 6-month survival rates are >80%. Current indications for surgery, as defined in the AHA and ESC guidelines. The optimal timing of surgical intervention is also contentious [31]. Delaying surgery may allow a high risk of disease progression with valve destruction, abscess formation, heart block, embolic complications, and even death [32]. Early surgery differs significantly between European and U.S. guidelines. The most common indication to perform early operation in the IE is the development of heart failure. Severe valve regurgitation, even among asymptomatic patients, imposes a volume load on the left ventricle, which results in ventricular dysfunction for dilatation or hypertrophy and heart failure. In mitral valve regurgitation, the elevation of left atrial pressure leads to left atrial enlargement, atrial fibrillation, and pulmonary congestion. In patients who had not received emergency surgery, the outcomes are nefarious because of the progression to cardiogenic shock. The large vegetation that comprises the functionality of the entire valve can have a faster deterioration with the progression of hemodynamic instability. Once the diagnosis of IE has been ascertained and the indication for surgery is formulated, there currently appears to be no demonstrated benefit in delaying surgery. The choice to perform ED surgery in the first few hours or with a 48-hour delay depends on the evaluation of the endocarditis team but above all on the patient's clinic. Mortality is low in centers of excellence with high-level experience in the management of complex patients, although very often, especially in complex or repetitive cases, it is not possible to standardize surgical techniques.

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## References

[1] Miro JM, Ambrosioni J. Infective endocarditis: An ongoing global challenge. European Heart Journal. 2019;**40**(39):3233-3236. DOI: 10.1093/eurheartj/ehz694

[2] Benedicto A, Domínguez L. Endocarditis and cardiac device infections. In: Firstenberg MS, Lakshmanadoss U, editors. Advanced Concepts in Endocarditis (Chapter 7). London, UK: IntechOpen, Rijeka; 2021. DOI: 10.5772/intechopen.96909

[3] Cahill T, Baddour L, Habib G, et al. Challenges in infective endocarditis. Journal of the American College of Cardiology. 2017;**69**(3):325-344. DOI: 10.1016/j.jacc.2016.10.066

[4] Mack M, Lancellotti P, et al. Early surgery in infective endocarditis. Journal of the American College of Cardiology. 2020;**76**(1):41-42. DOI: 10.1016/j.jacc.2020.05.049

[5] Gomes A, Jainandunsing JS, van Assen S, van Geel PP, Sinha B, Gelsomino S, et al. A standardized approach to treat complex aortic valve endocarditis: A case series. Journal of Cardiothoracic Surgery. 2018;**13**(1):32. DOI: 10.1186/s13019-018-0715-8

[6] Ivanovic B, Trifunovic D, Matic S, Petrovic J, Sacic D, Tadic M. Prosthetic valve endocarditis—A trouble or a challenge? Journal of Cardiology. 2019;**73**(2):126-133. DOI: 10.1016/j.jjcc.2018.08.007. Epub 2018 Oct 30

[7] Salem M, Friedrich C, Saad M, Frank D, Salem M, Puehler T, et al. Active infective native and prosthetic valve endocarditis: Short- and long-term outcomes of patients after surgical treatment. Journal of Clinical Medicine. 2021;**10**(9):1868. DOI: 10.3390/jcm10091868

[8] Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta J-P, Del Zotti F, et al. Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). European Heart Journal. 2015;**36**(44):3075-3128. DOI: 10.1093/eurheartj/ehv319

[9] Nishimura A, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2017;**135**:e1159-e1195. DOI: 10.1161/CIR.0000000000000503

[10] Flynn CD, Curran NP, Chan S, Zegri-Reiriz I, Tauron M, Tian DH, et al. Systematic review and meta-analysis of surgical outcomes comparing mechanical valve replacement and bioprosthetic valve replacement in infective endocarditis. Annals of Cardiothoracic Surgery. 2019;**8**(6):587-599. DOI: 10.21037/acs.2019.10.03

[11] Habib G, Erba PA, Iung B, Donal E, Cosyns B, Laroche C, et al. Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: A prospective cohort study. European Heart Journal. 2019;**40**(39):3222-3232. DOI: 10.1093/eurheartj/ehz620. Erratum in: European Heart Journal 2020;41(22):2091

[12] Van Vlasselaer A et al. Native aortic versus mitral valve infective endocarditis:

A nationwide registry study. Open Heart. 2019;**6**

[13] Satriano UM, Nenna A, Spadaccio C, Pollari F, Fischlein T, Chello M, et al. Guidelines on prosthetic heart valve management in infective endocarditis: A narrative review comparing American Heart Association/American College of Cardiology and European Society of cardiology guidelines. Annals of Translational Medicine. 2020;**8**(23):1625. DOI: 10.21037/atm-20-5134

[14] Bin Abdulhak AA, Qazi AH, Tleyjeh IM. Workup and management of native and prosthetic valve endocarditis. Current Treatment Options in Cardiovascular Medicine. 2018;**20**(9):73. DOI: 10.1007/s11936-018-0668-1

[15] Chan V. When should infective endocarditis be treated with early surgical intervention? The Canadian Journal of Cardiology. 2018;**34**(9):1110-1111. DOI: 10.1016/j.cjca.2018.06.013. Epub 2018 Jun 30

[16] Olmos C, Vilacosta I, Habib G, Maroto L, Fernández C, López J, et al. Risk score for cardiac surgery in active left-sided infective endocarditis. Heart. 2017;**103**(18):1435-1442. DOI: 10.1136/heartjnl-2016-311093. Epub 2017 Apr 21

[17] Farag M, Borst T, Sabashnikov A, Zeriouh M, Schmack B, Arif R, et al. Surgery for infective endocarditis: Outcomes and predictors of mortality in 360 consecutive patients. Medical Science Monitor. 2017;**23**:3617-3626. DOI: 10.12659/MSM.902340

[18] Khan A, Aslam A, Satti KN, Ashiq S. Infective endocarditis post-transcatheter aortic valve implantation (TAVI), microbiological profile and clinical outcomes: A systematic review. PLoS One. 2020;**15**(1):e0225077. DOI: 10.1371/journal.pone.0225077

[19] Bjursten H, Rasmussen M, Nozohoor S, Götberg M, Olaison L, Rück A, et al. Infective endocarditis after transcatheter aortic valve implantation: A nationwide study. European Heart Journal. 2019;**40**(39):3263-3269. DOI: 10.1093/eurheartj/ehz588

[20] Erbel R. The new strategy in infective endocarditis: Early surgery based on early diagnosis: Are we too late when early surgery is best? Circulation. 2015;**131**(2):121-123. DOI: 10.1161/CIRCULATIONAHA.114.013872. Epub 2014 Dec 5

[21] Mastrobuoni S, Chan V, Ruel M. Early surgery for infective endocarditis. The New England Journal of Medicine. 2012;**367**(14):1365-1366; author reply 1366-7. DOI: 10.1056/NEJMc1209897

[22] Nasso G, Santarpino G, Moscarelli M, Condello I, Dell'Aquila AM, Peivandi AD, et al. Surgical treatment of valve endocarditis in high-risk patients and predictors of long-term outcomes. Scientific Reports. 2021;**11**(1):24223. DOI: 10.1038/s41598-021-03602-3

[23] Nappi F, Iervolino A, Singh SSA. The new challenge for heart endocarditis: From conventional prosthesis to new devices and platforms for the treatment of structural heart disease. BioMed Research International. 2021;**2021**:7302165. DOI: 10.1155/2021/7302165

[24] Cuervo G, Escrihuela-Vidal F, Gudiol C, Carratalà J. Current challenges in the management of infective endocarditis. Frontiers in Medicine (Lausanne). 2021;**8**:641243. DOI: 10.3389/fmed.2021.641243

[25] Gordon SM, Pettersson GB. Native-valve infective endocarditis—When does it require surgery? The New England Journal of Medicine.

2012;**366**(26):2519-2521. DOI: 10.1056/NEJMe1205453

[26] Liang F, Song B, Liu R, Yang L, Tang H, Li Y. Optimal timing for early surgery in infective endocarditis: A meta-analysis. Interactive Cardiovascular and Thoracic Surgery. 2016;**22**(3):336-345. DOI: 10.1093/icvts/ivv368. Epub 2015 Dec 17

[27] Benedetto U, Spadaccio C, Gentile F. A narrative review of early surgery versus conventional treatment for infective endocarditis: Do we have an answer? Annals of Translational Medicine. 2020;**8**(23):1626

[28] Antunes MJ. Mitral valve repair versus replacement for infective endocarditis. What is better in the "real world"? The Journal of Thoracic and Cardiovascular Surgery. 2018;**156**(4):1471-1472. DOI: 10.1016/j.jtcvs.2018.05.010. Epub 2018 May 28

[29] Zubarevich A, Zhigalov K, Osswald A, Arjomandi Rad A, Vardanyan R, Wendt D, et al. Essen-commando: How we do it. Journal of Cardiac Surgery. 2021;**36**(1):286-289. DOI: 10.1111/jocs.15140. Epub 2020 Oct 21

[30] Weltert L, Gaudino M. Commentary: Even simplified, it is still a commando operation. JTCVS Techniques. 2020;**4**:104-105. DOI: 10.1016/j.xjtc.2020.09.010

[31] Chen P, Chang C, Chuang Y, Chen I, Lin T. Modified commando procedure in complicated infective endocarditis—A case series. Journal of Cardiothoracic Surgery. 2021;**16**(1):79. DOI: 10.1186/s13019-021-01480-4

[32] Elde S, de Biasi A, Woo YJ, Burton É. A novel alternative to the commando procedure: Constructing a neo-aortic root by anchoring to the sewing ring of the replaced mitral valve. JTCVS Techniques. 2020;**4**:101-102. DOI: 10.1016/j.xjtc.2020.08.037. Epub 2020 Aug 28