CLINICAL MANAGEMENT OF THE INFECTIVE ENDOCARDITIS TODAY

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ABSTRACT

The aim of this review is to present current trend in the clinical management of the infective endocarditis (I.E.). This disease has still, to date high mortality. So it is, in spite of the most modern therapeutic approaches based on both the latest generation of antibiotics, and the application of the latest cardiac surgery.

Therefore, it is important to focus on the medical and surgical treatment options currently most widely accepted among those available today, on the basis of international consensus and clinical experience acquired so far on this subject. In this article are reviewed these therapeutic modalities.

The rapid and accurate diagnosis and prompt and proper implementation of integrated medical and surgical therapies are essential in order to be able to lower as much as possible the mortality of this severe disease.

Key words: Infective endocarditis (I.E.), I.E. clinical management, I.E. medical treatment, I.E. surgical treatment.

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Introduction

Infective endocarditis (IE) is still today a serious disease with an high mortality, even if it was much reduced by modifications in therapeutic management in the last decades. In fact this has been possible, on the one hand, from the forties, thanks to the advent of antibiotics, on the other hand, starting from the mid-fifties and up to the present day, with the growth and development of cardiac surgery. Moreover to date, following international consensus, the surgical indications are much larger than in the past.

IE and its complications are frequently not controlled enough by medical therapy alone. Is just exactly in these circumstances that surgical therapy plays a key- role in the treatment of IE. In fact, as is known, in such conditions, the antibiotic therapy alone is associated with a high mortality rate much higher of surgical therapy[1,2].

Regarding IE of native valve, surgery is reserved for patients that, despite given antibiotic therapy, develop severe complications. Therefore, haemodynamically severe valvular diseases caused by IE, especially with heart failure, should be treated surgically.

It is important to specify that, even during a cycle of effective antibiotic-targeted therapy, valvular lesions may progress to worse pathological situations, leading to the insidious onset of heart failure in a few weeks. It is therefore necessary to monitor constantly the clinical conditions, even after the defervescence of the patient, in order to note the first signs of heart failure, suggesting the indication

for surgery. In the case of resolution of the infection (apyrexia, stable normalization of inflammation markers, negativity of blood cultures, absence of vegetations or abscesses), in the presence of valvular lesions haemodynamically not more than moderate, the patient may be placed in the clinical-instrumental follow-up after of the prescribed period of antibiotic therapy. More than 50% of the subjects in follow-up will require a valve replacement surgery within 10-15 years from the episode of IE[3].

Different are the clinical features of infective endocarditis in prosthetic valves. Like all infections, arising in the presence of a foreign body, prosthetic valve endocarditis are extremely difficult to eradicate with medical therapy alone, due to the development of a biofilm that isolates the bacteria from antibiotics and to the occurrence of bacterial genetic mutations that confer antibiotic resistance[4]. Therefore prosthetic IE, in most cases, requires surgical treatment[5].

Particularly aggressive turn out to be the early infections, which appear within three months, following implantation of the prosthesis and are usually caused by Staphylococcus aureus. These are frequently associated with the detachment of the prosthesis and the formation of abscesses. In these circumstances, with medical therapy alone mortality is extremely high, exceeding 50%[6,7].

Occasionally prosthetic IE caused by little aggressive bacteria and sensitive to antibiotics such as Streptococcus spp, can be treated with medical therapy alone in the absence of prosthesis detachment of relevant entities. However, a strict follow-up is advisable in this patients, with frequent echocardiographic monitoring, in order to capture time for the onset of complications.

Finally, surgical indication criteria are any pathological features associated with a particularly aggressive infection, such as: vegetations of diameter > 10 mm, recurrent systemic embolization (> 2 episodes) in the presence of vegetations, abscesses and perivalvular intracardiac fistulae, as not curable with antibiotic therapy alone.

On the other hand, it is reported in the literature that medical treatment alone is successful in patients with a limited extension of perivalvular infection, abscess with a diameter <1 cm and in any case in the absence of further complications such as atrio-ventricular block and severe valvular dysfunction[8].

It is worth pointing out, however, that these cases are extremely selected and subjected to frequent controls using transesophageal echocardiography, even after the end of antibiotic therapy cycle.

Indications and timing for surgical treatment

In principle, the surgical treatment of valvular lesions caused by IE should be deferred until the "cooling" of the infection status. This cooling is obtained through a parenteral antibiotic targeted therapy, for at least two weeks, with periodic close monitoring of inflammation markers (C-reactive protein, erythrocytes sedimentation rate) and blood cultures examination. Under ideal conditions, the surgery is performed in a stable afebrile patient, with blood cultures now negative and inflammatory markers in significant reduction.

The objective of the cooling is to operate on cardiac tissues reclaimed from the micro-biological point of view, in order to minimize the risk of IE recurrence, whose impact is of particularly unfavorable prognosis after implantation of a prosthetic valve. It is also desirable to wait for the normalization of renal function, frequently altered by antibiotics and by the formation of immune complexes that sometimes accompanies the IE.

However, the timing of choice is inappropriate in circumstances in which the infectious process appears to be extremely aggressive and even out of control. For example, in case of acute heart failure, mortality in medical therapy[9] can reach 51% and in any case is significantly higher than the consequent risks to a surgical valve replacement performed in active phase of IE, with an incidence of recurrence of infection on prosthesis no more than 3%[10]. In such situations, surgery must be carried out under urgency, or in extremely compromised patients, even emergency.

The indications for urgent surgery are represented by acute heart failure [class III-IV New York Heart Association (NYHA)], caused by severe valvular lesion, such as an high grade of aortic or mitral regurgitation. Acute heart failure is the most important prognostic factor in the IE[11,12].

In particular, acute aortic valvular regurgitation is the disease most frequently associated with severe acute heart failure followed by severe mitral insufficiency and from that tricuspid[9]. In the presence of massive and acute aortic regurgitation, the early closure of the mitral valve is an aggravating factor in the degree of heart failure and echocardiography should always be sought. They can also put to acute heart failure large prosthesis detachments

more than 40% of the circumference of the prosthetic anulus, the prosthetic malfunction by locking a movable element due to the presence of an infected thrombus, and fistulas created between the aortic root and the left atrium.

Other conditions may suggest the possibility of a early surgery, if not urgent, such as fungal endocarditis, Gram-negative (Serratia marcescens and Pseudomonas aeruginosa) and so considered "hard" germs (Brucella spp.), infection with antibiotic-resistant germs (Enterococcus spp.), persistent fever even in the presence of negative blood cultures (negative blood cultures endocarditis), perivalvular abscess, and persistent abscesses and vegetations and / or a septic state with positive blood cultures despite anti-biotic parenteral therapy lasting at least one week.

Specifically, the perivalvular abscess is associated with a particularly unfavorable prognosis in the short term, as it may predispose to more serious complications such as the atrio-ventricular block and fistula formation between the cardiac cavities. If an abscess is diagnosed, therefore, it is prudent rapidly to proceed surgically, in order to prevent the progression of the destructive endocarditic lesions and related complications. Finally, the detection of echocardiographic moving valvular vegetations, with a diameter > 10 mm, especially if located on the anterior leaflet of the mitral and / or with an increasing diameter, despite antibiotic therapy, is associated with an increased risk of systemic embolization, especially during the first two weeks of parenteral antibiotic therapy.

The use of an aggressive approach to the removal of such vegetations in early stage must be individualized, having to take into account, on the one hand, the operative risk, incremented during the active phase of the IE and, on the other hand, the risk of major embolization events, the more in the case of abstention from. In the case of valvular vegetations, it is advisable to work early, especially when coexist other conditions that require early treatment, such as perivalvular abscess or a persistent septic status.

Lately it has been suggested to operate prematurely patients suffering from mitral IE, particularly with involvement of the anterior leaflet, in order to increase the chances of feasibility of a conservative procedure, because performed before the lesions evolve to the point to result in the replacement of the valve with a prosthesis[13-15].

This approach appears very attractive, since it allows to avoid the prosthetic implant in many patients, thereby reducing the complications to it relate both short (relapse of IE) and long-term (thromboembolism, hemorrhage during anticoagulant therapy, prosthetic dysfunction).

Finally, it is important to consider the circumstances which make it necessary to delay the intervention.

The occurrence of an embolic cerebral infarction, especially if considerable extent, requires to postpone the cardiac operation of at least 14 days, in order to reduce the risk of intracranial hemorrhage associated with systemic heparinization, necessary for the extracorporeal circulation[16]. In the case of hemorrhagic stroke, it is advisable to extend the postponement for at least 28 days[17].

At the end of this period, the patient should be re-submitted to cerebral computed tomography (CT) in order to assess the state of the necrotic area, eventual hemorrhagic evolution and the presence of intracranial mycotic aneurysms.

The diagnosis of splenic abscess involves the need for a splenectomy, which ideally should be performed prior to cardiac surgery, in order to reduce the incidence of post-operative bacteremia and, consequently, the risk of prosthetic IE.

In patients at higher operative risk splenectomy may be performed laparoscopically[18] or even replaced by drainage through a percutaneous puncture[19].

General principles of surgery

Specific antibiotic therapy remains an essential component of the treatment of IE. However, in relation to the timeliness of diagnosis, the beginning of antibiotic therapy policy, the virulence of the causative microorganism and the involved cardiac structure (native valve or prosthetic valve), surgery may be necessary to save the patient's life and eradicate the infection. The timing of surgery, as already said, is crucial in cases when medical treatment is ineffective and delayed surgical therapy may result in an increase of the probability of complications and, therefore, a greater risk of surgical mortality and morbidity.

In this context, the notion that less virulent microorganisms such as *Streptococcus Viridans*, always respond to antibiotic treatment alone, may be erroneous, because infection due to these bacteria can cause significant damage to the heart valves

and surrounding structures, if not properly and promptly treated[20].

The two primary objectives of the cardiac intervention in the course of IE are:

• the eradication of the infective process, by the complete removal of the infected and necrotic tissues;

• the restoration of the anatomy and function of the involved cardiac structures.

Surgical treatment includes, regardless of the technique used, a first phase, demolitive, and subsequently a reconstructive phase. In demolitive step, the surgeon removes the more radically possible tissue or prosthetic material site of infection. One or more samples are sent to microbiology for culture. Is then performed the curettage of any abscesses and recesses and application of topical antibiotic and or antiseptic solutions on residual structures and surgical materials to be used. The proper implementation of this first step of the surgical treatment of IE plays a crucial role in its success, also understood in terms of preventing recurrence.

The general principles of the subsequent reconstructive phase are:

• using the least amount of inert prosthetic or heterologous material,

• use of autologous pericardium segments, vital to the reconstruction, if available,

• obliteration of each pathological cavity or recess;

• restoration of valve function using reconstruction (best treatment option) or prosthetic replacement.

The valve repair is the technique of choice, rather than the substitution, as:

• allows the preservation of anatomical and functional living cardiac structures;

• requires the introduction of a reduced amount of prosthetic inert material;

• reduces the long-term risk of thromboembolism and the risk of hemorrhage related to anticoagulant therapy imposed by the prosthesis;

• reduces the risk of recurrence of IE.

However, the use of reparative techniques is limited by:

• the level and location of the loss of substance as a result with IE and the surgical debridement,

• tolerance of the long intraoperative myocardial ischemia often imposed by complex reconstructions;

• surgeon experience.

Although the topic is debated, there is no evidence that biological prosthetic heart valves are associated with a lower risk of endocarditic relapse compared to mechanical prosthesis[21,22]. In part, this is also related to the fact that it is difficult to perform controlled studies, given the heterogeneity of clinical presentations of the disease and the anatomical conditions observed on the operating table. The literature is, however, rich in regard to the choice of prosthetic valve replacement, biological or mechanical, with more or less favorable results[23,24].

In general, the bioprosthesis, regardless of the age of the patient, are advisable in the event of the presence of co-pathologies particularly unfavorable in terms of long-term prognosis (i.e. severe left ventricular dysfunction), difficulty in the management of post-operative anticoagulation or contraindications to it. The valve replacement with mechanical prosthesis is usually carried out in patients with uncomplicated IE, in the absence of risk factors and contraindications to anticoagulant therapy, which must be continued for life.

Regardless, however, the surgical technique used, the ultimate success of the treatment of patients with IE cannot ignore the continuation of antibiotic therapy for this, which will be continued in the postoperative phase for a period of up to eight weeks. Over the years, the outcome of IE is significantly improved compared to the past.

This is the result of multiple factors, which include:

• the increased experience of the surgeon;

• effective myocardial protection;

• better management of perioperative bleeding;

• the aggressive debridement of infected tissue and prosthetic material;

• refinement of reconstructive and conservative surgical techniques;

• the availability of various types of prosthetic heart valves;

• use of intraoperative transesophageal echocardiogram (TEE), which allows accurate diagnosis of the site and extent of the infection and the assessment of the outcome of the surgical procedure;

• the variety and effectiveness of antibiotics on the market.

Particular aspects in relation to the valve affected by IE

Infective endocarditis of the aortic valve

When the infection is limited to the cusps of the native aortic valve or a biological valve prosthesis, causing perforation, breakage or malfunction, the complete removal of the valve and the implantation of a bioprosthesis or mechanical prosthesis generally solve the problem. Are quite unusual in surgical practice the reparative techniques in case of IE in the aortic position due to the small amount of valvular tissue available to the surgeon. If the IE involves the aortic anulus, is necessary accurate resection of the infected area before implanting the prosthetic valve.

For the reconstruction of the loss of substance created by debridement surgery, some surgeons prefer to use autologous pericardium, taken from the patient, in the case of small defects (1 or 2 cm) at the level of the aortic root and left ventricular outflow tract (LVOT). It employs a patch of heterologous pericardium (bovine), fixed with glutaraldehyde and suitably shaped, in order to reconstruct the more extensive loss of substance[25]. The literature also describes the reconstruction of the aortic root by Dacron patch[26,27].

Many surgeons feel that the *homograft* represents the ideal substitute for the reconstruction of the aortic root and of the LVOT, in cases of IE complicated by the formation of a perianular abscess, both of native valve that of prosthetic valve[28-33]. The reason for this lies mainly in the high versatility shown by the homograft in clinical conditions such as that described, in which it provides a more or less extended and complex reconstruction of the cardiac structures involved.

The ring of this prosthesis is not as rigid as that of common valved with Dacron conduits, it has a decent amount of muscle tissue and mitral valve tissue, which can be used to reconstruct extensive loss of substance at the level of the native anulus and LVOT. The use of this aortic valve homograft allows, at least in part, to simplify complex reconstruction procedures performed in the past, with satisfactory results. However it should be considered that the availability of the homografts is obviously much more limited than with other prostheses. Furthermore, as other prostheses, also this valvular substitute can be the target of the infectious process and after its implantation, in cases of IE, is described in different patient series, persistence or recurrence of the infection[34-36]. This is a demonstration of the fact that the success of the surgical therapy of the IE depends more on the skill of the surgeon in the removal of all infected tissues than type of valve prosthesis implanted. In the case of destructive IE, with extensive involvement of the aortic root and surrounding structures, in the presence of abscesses and /or intracardiac fistulas, surgical treatment is particularly "technically demanding". These patients frequently require the replacement of the aortic root and the reconstruction of the structures involved in the infectious process. Surgical procedures to be performed must be always individualized, since the extent of infection is variable from case to case.

Several authors have described the use of surgical techniques, alternative to the use of these valve substitutes in cases of IE on native or prosthetic aortic valve. Among these methods, we mention the stent-less aortic bioprosthesis, in which there is no rigid support that characterizes the conventional prosthetic valves. The use of these prostheses, characterized by versatility and ability to adapt also to extensively damaged native rings by the infectious process, as well as high hemodynamic performance, in different series has demonstrated good results, similar to those of the homograft[37,38].

Some surgeons prefer to use a pulmonary artery autograft in cases of extensive destruction of the aortic root, particularly mind in younger patients. This intervention is auto-transplantation of the pulmonary valve, a complex technique described by Donald Ross over 40 years ago[39,40]. Actually there is not a great experience using this technique in the treatment of IE, but in some cases are reported satisfactory results[40]. However, the real role of the Ross operation in the treatment of the IE still needs to be well defined. It is, moreover, of a technically complex procedure, the repeatability of which is rather limited.

Infective endocarditis of the mitral valve

Surgical treatment follows the same general principles described above: evaluation of the optimal timing, accurate preoperative diagnosis by TEE, radical removal of infected tissue, reconstruction of cardiac structures involved by the endocarditic process or using, as appropriate, repair or replacement of the mitral valve, appropriate post-surgery antibiotic treatment. One of the main differ-

ences with respect to the treatment of IE in the aortic site consists in surgical exposure of the mitral valve, which is often more difficult, especially in cases of reoperation. In addition, radical surgical debridement in cases of "complicated" IE, i.e. with the extension of the infectious process in the atrio-ventricular groove and formation of an abscess (with possible perforation of the base of the heart), it is generally more technically difficult than infection involving the aortic root.

Both options, as said, are the techniques of valve repair (which, unlike IE of aortic valve - policy, in case of IE of native mitral valve are the methods of choice) and replacement with prostheses. In the case of IE on native mitral valve, is the favorite, if possible, running repair techniques. Indispensable condition, but often satisfied, for the execution of a correct reconstruction of the valve, in addition to the experience of the cardiac surgeon, is the presence of residual valvular tissue after the debridement[41-45]. In case of extensive destruction of the subvalvular apparatus, it will replace the mitral prosthesis.

The anterior leaflet of the mitral valve may occasionally be involved in the endocarditic process originating from the aortic valve, with the formation of so-called drop lesions. These are typically the result of vegetation, capable of causing the corrosion and piercing of valve tissue. The reconstruction is performed using a patch of autologous or heterologous pericardium (treated with glutaraldehyde) sutured to the remaining tissue of the anterior leaflet. If indicated, the procedure is completed by the installation of a prosthetic ring.

If the infectious process has led to a rupture of chordae tendineae, the main described techniques are: transposition of the strings from the posterior valve leaflet or transfer secondary cords to the free margin of the anterior leaflet, or use of artificial chords.

The middle portion (segment P2) of the posterior leaflet is frequently involved by the infectious process. Among the reconstructive methods there is the quadrangular resection of P2, followed by the restoration of the continuity of the leaflet itself by direct suture of the remaining portions. In the case of presence of sufficient residual valvular tissue, also, may be made of a posterior sliding plastic procedure.

Generally the operation is completed by means of the implantation of a prosthetic ring or an incomplete ring. In case of extensive destruction of the posterior mitral annulus, it is necessary to carry out the removal of all non-viable tissue and reconstruction using ring segments of pericardium. If it is necessary to replace the valve, the mitral prosthesis, biological or mechanical, is sutured to the new ring reconstructed from the patch[41-44].

In the case of IE of mitral valve prosthesis, it is crucial from the technical point of view the achievement of an optimum exposure of the mitral valve. Once obtained the exposition of the mitral infected prosthesis, it is removed, with all the infected material. Rather common is the formation of an abscess cavity that by the valve annulus extends posteriorly, at the level of the atrio-ventricular groove, causing a variable degree of prosthetic detachment and a left atrio-ventricular discontinuity. In these situations, the strategic surgical strategy consists usually in the debridement of the annulus and its subsequent reconstruction using autologous or bovine pericardium fixed with glutaraldehyde (David technique)[45]. Through this method, a semi-circular patch of pericardium is sutured to the endocardium of the left ventricle and left atrium, thus obliterating the loss of substance and reconstructing the anulus on which will be implanted the new prosthetic valve.

When the endocarditic process extends into the intervalvular fibrous trigone, it may be necessary to replace both mitral and aortic valve, after reconstruction of the trigone itself. In these circumstances, the debridement is done removing as widely as possible the fibrous trigone, which is then reconstructed by autologous or heterologous pericardium. This tissue will thus provide the necessary support for the implant of the two new prosthetic valves[46].

Infective endocarditis of the tricuspid valve

In case of extended involvement of tricuspidalic valvular apparatus by the endocarditic process and in the absence of concomitant severe pulmonary hypertension, can be carried out a surgical approach in two stages, spaced by an interval of time varying from a few months to years. In the first step, you run the complete removal of all of the tricuspid valve and the infected tissue In these conditions, the blood circulates through the right cardiac sections without being guided by a unidirectional atrio-ventricular valve. After eradication of the infection through antibiotic therapy, will be performed the second surgical procedure, consisting in implantation of a prosthetic valve in the tricuspid

position[47-49]. If the infection is related to the intake of intravenous drugs, replacement of the tricuspid valve should preferably be carried out after the complete control of drug addiction. The repeated abuse of drugs, in fact, is directly related to survival rate at distance and at the rate of recurrence of IE after implantation of a prosthesis in the tricuspid position. A surgical approach one-stage for the treatment of IE of the tricuspid valve may instead be proposed in cases of less extensive infection and consists, after the accurate debridement, in the replacement or, if possible, in the valve repair[50-54].

Choice of valve prosthesis, biological or mechanical, in tricuspid position, follows the same general principles considered for valve replacement in mitral or aortic position. However, given the non-negligible risk of thrombosis in the right heart chambers, generally bioprosthesis are preferred in tricuspid position[50-54].

Conclusion

During the past decade, in order to reduce high mortality of IE, surgical indications have greatly increased, so we have entered into the era of early surgery[55,56]. Although aggressive therapy has become indispensable to save lives and to eradicate infection in many patients, reported rates of surgery remain heterogeneous, and the beneficial effect of surgery on mortality is still difficult to show. These difficulties result from the scarcity of randomized trials and several confounding factors that hamper the analysis of observational studies. Nevertheless, the results from most investigations are favorable for early surgical management in complicated infective endocarditis[55,56]. Thus, an appropriate identification of high-risk patients and their quick transfer to specialized medical-surgical centers seem to be crucial to improve the prognosis. Indeed, standardized management by a skilled multidisciplinary team has proven to decrease significantly mortality[56,57]. Despite this trend in treatment, most centers report an in-hospital fatality rate of about 20%, possibly because many patients are referred too late medical-surgical institutions that are experienced in infective endocarditis[56,57]. Therefore, challenges in management of this disease include improvement of diagnostic strategies to reduce delays for the start of appropriate treatment, better identification of patients who require close monitoring and urgent surgery, and development of both medical and surgical therapeutic methods[56,57].

According all international clinical experiences, in conclusion, we can say without any doubt that a rapid diagnosis of the disease and an appropriate identification of high-risk patients with their quick transfer to specialized centers is crucial to improve the prognosis.

References

1) Karchmer AW. *Infective Endocarditis*. In: Bonow RO, Mann DL, Zipes D P, Libby P, eds. In: Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 9th Ed. Philadelphia; Elsevier Saunders 2012: *1540-1558*.
2) Morris AJ, Drinkovic D, Pottumarthy S, Stricken MG, MacCulloch D, Lambie N, et al. *Gram stain, culture, and histopathological examination findings for heart valves removed because of infective endocarditis*. Clin Infect Dis 2003; 36: *697-704*.
3) Tornos MP, Olona M, Permanyer-Miralda G, Almirante B, Evangelista A, Soler-Soler J. *Long-term complications of native valve infective endocarditis in non-addicts: a 15-year follow-up study*. Ann Intern Med 1992; 117: *567-72*.
4) Padera RF. *Infection in ventricular assist devices: the role of biofilms*. Cardiovasc Pathol 2006; 15: *264-70*.
5) Karchmer AW. *Infections of prosthetic heart valves*. In: Waldvogel F, Bisno AL, eds. In: Infections Associated with indwelling medical devices. 3 rd ed. Washington, DC: Edit by American Society for Microbiology 2000: *145-72*.
6) Chirouze C, Cabell CH, Fowler VG Jr, Khayat N, Olaison L, Miro JM, et al. *Prognostic factors in 61 cases of Staphylococcus aureus prosthetic valve infective endocarditis from the International Collaboration on Endocarditis merged database*. Clin Infect Dis 2004; 38: *1323-7*.
7) Sohail MR, Martin KR, Wilson WR, Baddour LM, Harmsen WS, Stcckelberg JM. *Medical versus surgical management of Staphylococcus aureus prosthetic valve endocarditis*. Am J Med 2006; 119: *147-54*.
8) Rohmann S, Seifert T, Erhel R, Jakob H, Mohr-Kahaly S, Makowski T, et al. *Identification of abscess formation in native-valve infective endocarditis using transesophageal echocardiography: implications for surgical treatment*. Thorac Cardiovasc Surg 1991; 39: *273-80*. Sexton DJ, Spelman D. *Current best practices and guidelines: assessment and management of complications in infective endocarditis*. Cardiol Clin 2003; 21: *273-82*.
9) Sexton DJ, Spelman D. *Current best practice and guidelines: assessment and management of infective endocarditis*. Cardiol Clin 2003; 21: *273-82*.
10) Mills J, Utley J, Abbott J. *Heart failure in infective endocarditis: predisposing factors, course and treatment*. Chest 1974; 66: *151-57*.
11) Stinson EB. *Surgical treatment of infective endocarditis*. Prog Cardiovasc Dis 1979; 22: *145-68*.

12) Vikram HR, Buenconsejo J, Hasbun R, Quagliearello VJ. *Impact of valve surgery on 6-month mortality in adults with complicated, left-sided native valve endocarditis: a propensity analysis*. JAMA 2003; 290: *3207-214*.
13) El-Khoury G. *Surgery in endocarditis - whom to operate and when: new techniques for aortic valves*. Paper presented at the 7th International Symposium on Modern Concepts in Endocarditis and Cardiovascular Infections, Chamonix, France, June 2003; *26-28*.
14) Dion R. S*urgery in endocarditis - whom to operate and when: new techniques for mitral valves*. Paper presented at the 7th International Symposium on Modern Concepts in Endocarditis and Cardiovascular Infections, Chamonix, France, June 2003; *26-28*.
15) Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Barwolf C, Levang OW, et al. *A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on Valvular Heart Disease*. Eur Heart J 2003; 24: *1231-43*.
16) Ting W, Silverman N, Levistky S. *Valve replacement in patients with endocarditis and cerebral septic emboli*. Ann Thorac Surg 1991; 51: *18-21*.
17) Gillinov AM, Shah RV, Curtis WE, Stuart RS, Cameron DE, Baumgartner WA. Valve replacement in patients with endocarditis and acute neurologic deficit. Ann Thorac Surg 1996; 61: *1125-30*.
18) Simsir SA, Cheeseman SH, Lancey RA, Vander Salm TJ, Gammle JS. *Staged laparoscopic splenectomy and valve replacement in splenic abscess and infective endocarditis*. Ann Thorac Surg 2003; 75: *1635-7*.
19) Lerner RM, Spataro RE *Splenic abscess: percutaneous drainage*. Radiology 1984; 153: *643-45*.
20) D'Udekem Y, David TE, Feindel CM, Armstrong S, Sun Z. *Long-term results of operation for paravalvular abscess*. Ann Thorac Surg 1996; 62: *48-53*.
21) Moon MR, Miller DC, Moore KA, Oyer PE, Mitchell RS, Robbins RC et al. *Treatment of endocarditis with valve replacement: the question of tissue versus mechanical prosthesis*. Ann Thorac Surg 2001; 71: *1164-71*.
22) Hammcrmeister K, Sethi GK, Henderson WG, Grover FL, Oprian C, Rahlmtoola SH. *Outcomes 15 years after valve replacement with a mechanical versus a bioprosthetic valve: final report of the Veterans Affairs Randomized Trial*. J Am Coll Cardiol 2000; 36: *1152-58*.
23) Banbury MK, Cosgrove DM, Thomas JD, Blackstone EH, Rajeswaran J, Okies JE, et al. *Hemodynamic stability during 17 years of the Carpentier-Edwards aortic pericardial bioprosthesis*. Ann Thorac Surg 2002; 73: *1460-65*.
24) Guerra JM, Tornos MP, Permanycr-Miralda G, Almirante B, Murtra M, Soler-Soler J. *Long-term results of mechanical prostheses for treatment of active infective endocarditis*. Heart 2001; 86: *63-8*.
25) David TE, Komeda M, Brofman PR. S*urgical treatment of aortic root abscess*. Circulation 1989; 80 Suppl 1: *269-74*.
26) Jault F, Gandjbakhch I, Chastre JC, Levasseur IP, Bors V, Gibert C, et al. *Prosthetic valve endocarditis with ring abscesses: surgical management and long-term results*. J Thorac Cardiovasc Surg 1993; 105: *1106-13*.
27) Fiore AC, Ivey TD, McKcown PR Misbach GA, Allen MD, Dillard DH. *Patch closure of aortic annulus mycotic aneurysm*. Ann Thorac Surg 1986; 42: *372-9*.
28) Haydock D, Barratt-Boyes B, Macedo T, Kirklin JW, Blackstone E. *Aortic valve replacement for active infective endocarditis in 108 patients: a comparison of free-hand allograft valves with mechanical prostheses and bioprostheses*. J Thorac Cardiovasc Surg 1992; 103: *130-9*.
29) Yankah AC, Pasic M, Hose H, Siniawski H, Weng Y, Hetzer R. *Homograft reconstruction of the aortic root for endocarditis with periannular abscess: a 17-year study*. Eur J Cardiothorac Surg 2005; 28: *69-75*.
30) Grinda JM, Mainardi IL, D'Attellis N, Bricourt MO, Berrebi A, Fabiani JN, et al. *Cryopreserved aortic viable homograft for active aortic endocarditis*. Ann Thorac Surg 2005; 79: *767-71*.
31) Glazier JJ, Verwilghen J, Donaldson RM, Ross DN. *Treatment of complicated prosthetic aortic valve endocarditis with annular abscess formation by homograft root replacement*. J Am Coll Cardiol 1991; 17: *1177-82*.
32) Dossche KM, Defauw JJ, Ernst SM, Craenen TW, De Jongh BM, de la Riviere AB. *Allograft aortic root replacement in prosthetic aortic valve endocarditis: a review of 32 patients*. Ann Thorac Surg 1997; 63: *1644-9*.
33) Knosalla C, Weng Y, Yankah AC, Siniawski H, Hofmeister J, Hammer-schmidt R, et al. *Surgical treatment of active infective aortic valve endocarditis with associated periannular abscess - 11 year results*. Eur Heart J 2000; 21: *490-7*.
34) Kilian E, Oberhoffer M, Gulbins H, Uhlig A, Kreuzer E, Reichart B. *Ten years' experience in aortic valve replacement with homografts in 389 cases*. J Heart Valve Dis 2004; 13: *554-9*.
35) Ritter M, von Segesser L, Lenni R. *Persistent root abscess after emergency repair with an aortic homograft*. Br Heart I 1994; 72: *495-7*.
36) Joyce FS, McCarthy PM, Stewart WJ, Tomford JW, Rehm SJ, Heupler FA, et al. *Left ventricle to right atrial fistula after aortic homograft replacement for endocarditis*. Eur J Cardiothorac Surg 1994; 8: *100-2*.
37) Muller LC, Chevtchik O, Bonatti JO, Muller S, Fille M, Laufer G. *Treatment of destructive aortic valve endocarditis with the Freestyle Aortic Root Bioprosthesis*. Ann Thorac Surg. 2003; 75: *453-6*.
38) Siniawski H, Lehmkuhl H, Weng Y, Pasic M, Yankah C, Hoffmann M, et al. *Stentless aortic valves as an alternative to homografts for valve replacement in active infective endocarditis complicated by ring abscess*. Ann Thorac Surg 2003; 75: *803-8*.
39) Ross DN. *Replacement of aortic and mitral valves with a pulmonary auto-graft*. Lancet 1967; 2: *956-8*.
40) Oswalt JD, Dewan SJ, Mueller MC, Nelson S. *Highlights of a ten-year experience with the Ross procedure*. Ann Thorac Surg 2001; 71 (5 Suppl): S332-5.
41) Dreyfus G, Serraf A, Jebara VA, Deloche A, Chauvaud S, Couetil IP, et al. *Valve repair in acute endocarditis*. Ann Thorac Surg 1990; 49: *706-11*.
42) Hendren WG, Morris AS, Rosenkranz ER, Lyde BW, Taylor PC, Stewart WJ, et al. *Mitral valve repair for bacterial endocarditis*. J Thorac Cardiovasc Surg 1992; 103: *124-8*.
43) Muehrcke DD, Cosgrove DM 3 rd , Lytle BW, Taylor

PC, Burgar AM, Dumwald CP, el al. *Is there an advantage to repairing infected mitral valves?* Ann Thorac Surg 1997; 63: *1718-24*.
44) Lytle BW: *Prosthetic valve endocarditis*. In: Vlessis AA, Bolling SF, eds. Endocarditis: a multidisciplinary approach to modern treatment. Armonk, NY: Futura Publishing; 1999: *344-75*.
45) David TE, Feindel CM, Armstrong S, Sun Z. *Reconstruction of the mitral annulus: a ten-year experience*. J Thorac Cardiovasc Surg 1995; 110: *1323-32*.
46) David TE, Kuo J, Armstrong S. *Aortic and mitral valve replacement with reconstruction of the intervalvular fibrous body*. J Thorac Cardiovasc Surg 1997; 114: *706-71*.
47) Arbulu A, Thorns NW, Wilson RI. *Valvulectomy without prosthetic replacement: a lifesaving operation for tricuspid Pseudomonas endocarditis*. J Cardiovasc Surg 1972; 74: *103-7*.
48) Lai D, Chard RB. Commissuroplasty. *A method of valve repair for mitral and tricuspid endocarditis*. Ann Thorac Surg 1999; 68: *1727-30*.
49) Walther T, Falk V, Schneider J, Walther C, Mohr FW. *Stentless tricuspid valve replacement*. Ann Thorac Surg 1999; 68: *1858-9*.
50) Arneborn P, Bjork. VO, Rodriquez I, Svanbom M. *Two-stage replacement of tricuspid valve in active endocarditis*. Br Heart J 1977; 39: *1276-8*.
51) Wright JS, Glennie IS. *Excision of tricuspid valve with later replacement in endocarditis of drug addition*. Thorax 1978; 33: *518-9*.
52) Yee ES, Khonsari S. *Right-sided infective endocarditis: valvuloplasty, valvectomy or replacement*. J Cardiovasc Surg 1989; 30: *744-8*.
53) Turley K. *Surgery of right-sided endocarditis: valve preservation versus replacement*. J Card Surg 1989; 4: *317-20*.
54) Van Nooten G, Caes F, Tacymans Y, Van Belleghem Y, Francois K, De Bacquer D, et al. *Tricuspid valve replacement: postoperative and long-term results*. J Thorac Cardiovasc Surg 1995; 110: *672-9*.
55) Tleyjeh IM, Abdel-Latif A, Rahbi H, et al. *A systematic review of population-based studies of infective endocarditis*. Chest 2007; 132: *1025-35*.
56) Thuny F, Habib G, *When should we operate on patients with acute infective endocarditis?* Heart 2010; 96: *892-897*.
57) Botelho-Nevers E, Thuny F, Casalta JP. *Dramatic reduction in infective endocarditis-related mortality with a management-based approach*. Arch Intern Med 2009; 169: *1290-98*.
58) Thuny F, Botelho E, Casalta JP, Gouriet F, Raoult D, Habib G, *Can we really achieve a 1-year mortality rate lower than 10% in patients with infective endocarditis?* Arch Intern Med 2010; 170: *211-12*.

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