# Rheumatic fever and valvular heart disease: which prosthesis is best?

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## 1 INTRODUCTION

Rheumatic fever is a disease that occurs after infection by group A ß-hemolytic streptococci, commonly generated by a pharyngitis condition (skin infections may also occur), thus being considered an acute inflammatory, multisystemic and autoimmune disease. Thus, rheumatic heart disease is the post-inflammatory result of rheumatic fever, and may have two main manifestations: valve stenosis, which consists of the failure of the valve to open, causing obstruction of blood flow, and valve insufficiency, which is the failure of the valve to close, generating blood reflux. These events mainly affect the left atrioventricular (mitral) valve.

Currently, the incidence of this disease has declined in most parts of the world due to improved socioeconomic conditions, diagnosis and treatment. However, this does not happen in underdeveloped and developing countries, such as Brazil, which highlights the need for further studies on this situation.

## 2 OBJECTIVE

Understand the relationship between Rheumatic Fever and Valvulopathies through the pathophysiological process of these diseases. In addition, analyze which is the best valve prosthesis, mechanical or biological, evaluating its durability and the need to use anticoagulants.

## 3 METHODOLOGY

This is a literature review, developed with articles published from 2018 to 2023 in the electronic databases: *Scientific Electronic Library Online* - Scielo and PubMed, using the descriptors: valvulopathies, rheumatic fever, streptococci, biological prostheses, mechanical prostheses and their respective synonyms and combinations between them, in Portuguese and English. Only published articles that addressed the topic and were available online were included. Articles outside the proposed period, that did not address the chosen theme, not available online, that were not bibliographic reviews and repeated articles found in different databases were excluded.

## 4 DEVELOPMENT

Rheumatic fever is a pathology that affects more vulnerable people, the main factors being genetic susceptibility, since there are genes responsible for controlling the innate immune response, adaptive immune response, cytokines and B-alloantigen cells, and the environment, in which socioeconomic conditions, such as hygiene and nutrition, have a great impact.

This disease basically consists of an autoimmune hypersensitivity response against group A ß-hemolytic streptococcus antigens, which generates a cross-reaction with the individual's own molecules. This reaction occurs mainly with heart cells, as antibodies that attack the M proteins present in streptococci also attack proteins in myocardial tissue and heart valves, generating a cytokine-mediated response. However, this condition can also reach other tissues such as skin and CNS, which underscores the severity of this disease (ROBBINS & Cotran, 2016).

Thus, rheumatic heart disease in its acute phase generates inflammatory foci and lesions, commonly called Aschoff nodules, which are accumulations of T cells, plasma cells and Anitschkow cells (enlarged and activated macrophages). During rheumatic fever, these nodules may be present in the epicardium, myocardium and endocardium, characterizing a picture of pancarditis. Consequently, the deposition of fibrin in these Aschoff nodules generates the so-called warts, which compromise the proper functioning of the heart (ROBBINS & Cotran, 2016).

Symptoms of rheumatic fever in the acute phase start about 2 or 3 weeks after infection and its diagnosis is made on the basis of the Jones criteria (carditis, migratory polyarthritis of the large joints, subcutaneous nodules, marginalized erythema on the skin and Sydenham's chorea). However, rheumatic heart disease is detected by Doppler echocardiography as it is more sensitive and specific. However, this equipment is rarely used in low-income populations because of its unaffordable value, which makes early diagnosis impossible and contributes to the more severe evolution of the disease, with irreversible valve damage, requiring surgical replacement (Branco et al, 2022).

In a more severe situation, chronic rheumatic heart disease occurs, a condition characterized by the presence of few or even no lesions, but there is the presence of excessive scarring, which can generate fibrosis and calcification, causing the valves to be compromised, resulting in valvulopathy. In chronic rheumatic disease (CRD), the fibrosis process is perpetuated throughout the progression of the disease. Thus, the valves continue to maintain the inflammatory process, mainly due to mononuclear cells (Gomes, Nayara F.A. et al, 2021, ROBBINS and Cotran, 2016).

Inflammatory intensity is related to the area of the valve itself and not to the thickness of its leaflet. In this sense, autoimmune inflammation occurs basically due to the binding of reactive antibodies to the valve endothelium, which, once activated, increases the presence of adhesion molecules, responsible for facilitating the binding of T cells in this region. In addition, this immune response is amplified, as there is a continuous presentation of autoantigens in this area. After the

activation of these T cells, the endothelium that protects the valve tissue ends up being ruptured due to the presence of antibodies and/or inflammatory cytokines, allowing the healing process to take place. In this way, interstitial cells in this region can differentiate into myofibroblasts that, when activated and proliferating, generate inflammatory proteins and numerous cytokines, being responsible, in short, for the formation of fibrosis, which makes the healing process more intense in the valve region.(Gomes, Nayara F.A et al,2021).

In this context, calcification of the valves also occurs, which, although not a fully clarified process, has some relevant hypotheses, one of which states that the deposition of minerals is more prevalent in areas of neoangiogenesis, which are related to this inflammation and to the expression of vascular endothelial growth factor (VEGF), responsible for bone remodeling (stimulates the differentiation of osteoblastic cells). In addition, studies indicate that the presence of extracellular vesicles, derived from smooth muscle cells and valve interstitial cells, also contribute to this process, since they produce the substances osteopontin and osteocalcin, which have a mechanism of action similar to osteoblasts. (LEAL, M. T. B. C. et al,2019)

The main valve affected is the mitral valve, since its valves become thickened, with fusion and shortening of the commissures and fusion and thickening of the chordae tendineae, making its proper functioning impossible. Valvular heart disease has two main consequences: stenosis and valve insufficiency. Stenosis is understood as the failure of the valves to open, causing an obstruction of blood flow, while valve insufficiency consists of the failure of the valve to close, which causes regurgitation of blood. In the case of CKD, stenosis is more prevalent and, when intense, can cause dilation of the left atrium which, consequently, can generate atrial fibrillation. This pathology can have the effect of thrombus formation, generating numerous systemic repercussions, an example being ischemic stroke, which can result in a sequela and relevant neurological deficit. (Wunderlich NC, Dalvi B, Ho SY, Küx H, Siegel RJ, 2019; ROBBINS & Cotran, 2016).

If detected at an early stage, treatment for rheumatic fever is relatively simple, as antibiotics are used. However, if this disease is not detected early or if prophylactic pharmacological treatment is not carried out correctly, this situation can evolve into a chronic condition of mitral stenosis or insufficiency, and the treatment is pharmacological and then surgical.

In the case of pharmacological treatment for mitral stenosis, therapy is used only to relieve symptoms, since it does not act on the valve problem itself. The main drugs used are diuretics, especially loop diuretics, which, in addition to relieving symptoms, are also recommended in the presence of pulmonary congestion. Surgical correction can be performed by replacement with mechanical and biological prostheses, grafts or valve plastic reconstruction. In the option of using biological prostheses, the advantage is that it does not require the use of anticoagulants, however, the duration of this prosthesis is shorter when compared to the mechanical one. The mechanical prosthesis

has a longer durability, but the use of anticoagulants is essential, which, if not used correctly, can cause bleeding or thrombosis.

Thus, surgical intervention can be performed by means of plastic reconstruction (preserves the structures of the native valve and maintains the shape and volume of the camera), replacement of the valve by prosthesis with partial or total preservation of adjacent structures (depends on the degree of injury and presence of calcification) and replacement by prosthesis with complete removal of the valve.

In mechanical valve replacement, pyrolytic carbon double leaflet disks are used. Despite their excellent durability, these prostheses require the constant use of anticoagulants and, if used inappropriately, can generate both bleeding and valve thrombosis. Biovalvar prostheses, which are made from bovine and porcine tissues, do not require anticoagulant therapy except in cases where there are associated risk factors, but they are not very durable and, over time, their functionality ceases to be efficient due to deterioration and loss of mobility. It is important to emphasize that both types of prostheses are susceptible to infection, and mechanical prostheses, for example, can generate infective endocarditis (Coffey PM, Ralph AP, Krause VL, 2018).

## 5 FINAL CONSIDERATIONS

In view of the findings in the literature, it is concluded that inadequate treatment of Rheumatic Fever can lead to a process of valve insufficiency or stenosis, mainly affecting the mitral valve, through an autoimmune reaction that affects the cardiac tissue. The treatment of these valvular changes is based on symptomatic, with the use of diuretics and vasodilators, and depending on the severity of the valvular condition, surgical procedures can be performed by replacing the diseased valve. Among the possibilities of replacement are mechanical and biological, the former requiring the use of anticoagulants and has long durability, while the latter are short-lived and do not require anticoagulation, except in cases of patients who are carriers of risk factors.

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