



## Conservative management and surgical approaches in the treatment of Peripheral Obstructive Arterial Disease (POAD): An overview

### Manejo conservador e abordagens cirúrgicas no tratamento de Doença Arterial Obstrutiva Periférica (DAOP): Uma *overview*

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#### ABSTRACT

**Introduction:** Peripheral Arterial Obstructive Disease (PAD) is a condition in which there is narrowing or blockage of the arteries that supply the lower limbs. The main objective of this systematic review was to identify studies that addressed the pathophysiology, epidemiology, and signs and symptoms of PAOD, with special emphasis on surgical intervention strategies. **Methods:** The search was conducted in renowned databases, such as PubMed, Scopus, SciELO, Cochrane Library, LILACS, UpToDate and Embase, using controlled descriptors from DeCS. To carry out the effective search of the studies, descriptors such as "Peripheral Arterial

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Disease", "Vascular Surgical Procedures", "Myocardial Revascularization", "Angioplasty", "Vascular Graft", "Thromboendarterectomy" and "Vascular Surgery" were used. These descriptors were combined with Boolean operators "OR" and "AND" to improve search accuracy. The methodological approach adopted allowed for a careful and comprehensive search, ensuring the inclusion of relevant studies. Results: The final sample consisted of 28 articles published in indexed scientific journals, addressing different aspects of PAOD, such as symptoms, epidemiology, and surgical approach. The articles were made available in full for analysis and were written in Portuguese. The analysis of the studies allowed us to better understand the pathophysiology of PAD, identify the main symptoms and examine the different surgical approaches used in the treatment. Conclusion: A comprehensive systematic review of the literature on PAOD provided valuable information about the disease and its surgical treatment modalities. The results obtained are essential to guide clinical practice and assist in decision-making regarding the management of PAD. The methodological approach adopted ensured the inclusion of relevant studies and provided a solid basis for understanding PAOD and providing appropriate care to patients.

**Keywords:** Peripheral Arterial Obstructive Disease, Surgical treatment, Vascular rehabilitation.

## INTRODUCTION

Peripheral Arterial Obstructive Disease (PAD) is a disease characterized by the narrowing and stiffening of the peripheral arteries that carry blood flow to the upper and lower limbs, as a result of an obstruction caused by an atheromatous plaque, as well as other substances, such as calcium.

This clinical condition is prevalent, especially in individuals from the fifth decade of life, and is associated with an increased risk of cardiovascular events<sup>1</sup>. Atherosclerosis, a systemic disease that develops over several decades and worsens with advancing age, is an important cause of PAOD<sup>2</sup>. Atherosclerosis is a pathological process that involves the formation of plaque within the walls of the arteries, leading to obstruction of blood flow. This process is complex and involves several steps, including endothelial dysfunction, inflammation, lipid accumulation and smooth muscle cell proliferation<sup>3</sup>.

Endothelial dysfunction is one of the first steps in the pathogenesis of atherosclerosis. This occurs when the balance between the production of vasodilator and vasoconstrictor substances by the endothelium is disturbed, leading to a greater tendency to vasoconstriction, inflammation, and thrombosis<sup>3</sup>.

In PAD, atherosclerosis is most commonly seen in the femoral and tibial arteries. When lesions develop in the leg and foot, the tibial arteries are the most commonly affected<sup>4</sup>.



The symptoms of PAOD can range from leg pain when walking (intermittent claudication) to pain at rest and wounds that do not heal in the most severe cases. PAOD is also associated with an increased risk of cardiovascular events, such as heart attack and stroke<sup>5</sup>.

The management of PAOD involves the management of risk factors, such as dyslipidemia, diabetes, smoking, and hypertension, as well as surgical or endovascular interventions in cases of critical limb ischemia<sup>6</sup>. Physical rehabilitation and regular exercise are also important parts of the management of PAD.

## **MATERIALS AND METHODS**

Initially, we conducted a comprehensive systematic review of the literature, using several renowned databases, such as PubMed, Scopus, SciELO, Cochrane Library, LILACS, UpToDate, and Embase. The primary objective of this review was to identify a broad set of studies that addressed Peripheral Arterial Obstructive Disease (PAD), encompassing its pathophysiology, epidemiology, signs and symptoms, with special emphasis on surgical intervention strategies.

For the effective search of manuscripts in these databases, we used controlled DeCS descriptors, including terms such as "Peripheral Arterial Disease", "Vascular Surgical Procedures", "Myocardial Revascularization", "Angioplasty", "Vascular Graft", "Thromboendarterectomy" and "Vascular Surgery". To improve search accuracy, we combine these descriptors with "OR" and "AND" Boolean operators. For example, we use formulations such as (Peripheral Arterial Disease OR PAOD) and (Vascular Surgical Procedures OR Vascular Surgery).

This methodological approach was adopted in order to cover a broad spectrum of information related to PAOD and its surgical treatment modalities. The strategic combination of databases and descriptors allowed for a careful and comprehensive search, ensuring the inclusion of relevant studies and providing a basis for systematic review.

The sample was composed of studies published in indexed scientific journals. Considering different perspectives, such as symptomatology, epidemiology, and surgical approach. Aiming at a higher quality of materials as methodological, resulting in the final sample with 28 articles to compose the references, published throughout the period, available in full for analysis and in the following languages: Portuguese, English and Spanish.



## RESULTS AND DISCUSSION

Regarding the pathophysiology, it should be considered that PAOD consists of atherosclerosis, and is characterized by endothelial dysfunction associated with the deposition of lipids, connective tissue elements – which form a fibrous plaque, smooth muscle cells, as well as inflammatory cells as well as elements such as calcium in the vascular system of the peripheral limbs<sup>1</sup>.

When talking about endothelial dysfunction, one must take into account the complexity involved in the formation of blood vessels, which are divided into tunics, or layers<sup>9</sup>. In the luminal or intimate part of the vessels, that is, the part in contact with the blood flow, most vessels have an endothelial layer formed by endothelial cells, united to elements of the connective tissue, such as collagen and also elastic fibers, and around this layer, there is the tunica media, composed of a thick layer of elastic laminae and smooth muscle cells. Finally, there is the adventitious tunic, formed mainly by connective tissue, with collagen, fibrocytes and fibroblasts.<sup>9,10</sup>

It should be noted that the endothelium is biologically active and acts by receiving information and translating it into signals through the production of chemical substances<sup>11</sup>. When changes are perceived by the endothelium, there is a response translated by the change in the mechanical tension of the vessels, leading to a change in the way blood flow is conducted, which goes from laminar to turbulent, as well as the production of metabolic substances that alter endothelial physiology. Thus, endothelial dysfunction is established<sup>9,10,11</sup>.

The next step of DAOP then is the formation of the plate. In the face of endothelial dysfunction, there will be an increase in the permeability of the tunica intima, which allows LDL, which is in high concentrations in the plasma, to infiltrate the endothelium and be deposited in the tunica intima. With this deposition, macrophage recruitment will occur, forming foam cells, and signaling an inflammatory response with LDL oxidation. However, the plaque undergoes a kind of maturation, which consists of the synthesis of fibrotic substances, forming a fibrous layer, so that it is stabilized. Thus, atherosclerosis is established and when the arteries affected by this whole process are peripheral, Peripheral Arterial Obstructive Disease occurs<sup>12,13,14</sup>.

When it comes to diseases involving atherosclerosis, it is well established in the literature that these are associated with several risk factors, the main ones being: age, smoking, diabetes mellitus (DM), systemic arterial hypertension (SAH), hyperlipidemia, family history, among others. It can be noted that PAOD has high morbidity and mortality. It has a prevalence of 10 to



25% in the population over 55 years of age, and increases with age and about 70 to 80% of patients affected by the disease are asymptomatic. It should also be noted that DM increases the risk of PAOD by 1.5 to 4 times, being associated with cardiovascular events and increased mortality, with a 20% association between PAOD and diabetes. Diabetic PAOD patients are at high risk of complications such as ischemic ulcers, gangrene, and are the most common cause of amputation.<sup>5,6,7.</sup>

Elevated total cholesterol level increases the risk of intermittent claudication by up to two-fold, hypercholesterolemia rates of 60% and 77% have been observed in patients with PAOD respectively. These high levels of cholesterol, low-density lipoproteins, and triglycerides are independent risk factors for the disease, with high-density proteins being protective factors. When talking about the association with SAH, about 52% have SAH, The risk of intermittent lameness in these patients is increased by 2.5 to 4 times, both in men and women. It is now known that there is a higher prevalence of PAOD in black and Hispanic patients, with blacks without Hispanic descent having a rate of PAOD three times higher than whites without Hispanic descent.<sup>5,6,7.</sup>

Smoking is the most important risk factor for PAD, as well as for the onset of its manifestations such as intermittent claudication and critical ischemia. It increases the risk of the disease by about four times and accelerates the onset of intermittent claudication by about a decade. When comparing the evolution of non-smoking PAOD patients with smokers, we observed in this group a lower survival rate due to cardiovascular events and worsening of limb ischemia, with amputation rates twice as high. The association between PAOD and smoking is twice as high when compared with coronary heart disease, and the reasons are not clearly known.<sup>7</sup>

A patient with chronic obstruction of the arteries of the legs may not have any symptoms (i.e., be asymptomatic) if this obstruction is small (partial) or the alternative circulation has developed significantly<sup>14,15</sup>. There may also be no symptoms if the patient has other limitations that do not allow arterial disease to manifest itself, as is the case with people with diabetic neuropathy.

However, the most common symptom of PAOD is intermittent claudication. However, non-invasive measures, such as the ankle-brachial index, show that asymptomatic PAOD is several times more common in the population than intermittent claudication. Intermittent claudication is considered a benign manifestation, due to the low risk of limb loss, of



approximately 1% per year. About 75% to 80% of patients remain stable or improve over time, especially if treated appropriately.<sup>5</sup>

The diagnosis of PAOD often involves imaging tests, such as computed tomography angiography (CTA) or Doppler ultrasound, which can provide information about the degree of arterial obstruction. Another diagnostic test is the ankle-brachial index (ABI), obtained from the ratio between the systolic pressure in the dorsal arteries of the foot and the plantar pressure in the systolic arteries of the brachial artery, using Doppler ultrasound. Atherosclerosis rarely reaches the arteries of the arms. The lower the measurement of pressure in the feet relative to the pressure of the arm, the more severe the ischemia. CT angiography combines the CT scan technique with angiography, thus allowing a more detailed study of the arteries of the limbs.<sup>5,15,16,17.</sup>

Computed tomography angiography (CTA) or magnetic resonance angiography (MRI) offer detailed images of the arteries, allowing for accurate identification of blockages.<sup>19,20.</sup> Another common test to confirm the diagnosis of PAOD is the treadmill test, which consists of the patient walking on a monitored treadmill to assess the distance traveled before the onset of claudication, helping to determine the degree of functional impairment.<sup>21</sup> Early diagnosis of PAOD is crucial to prevent complications, such as ulcers or gangrene.

Initial management of all patients with arterial disease should be clinical, with control of blood pressure, diabetes, cholesterol levels, and smoking cessation. Medications such as antiplatelet agents and statins are part of the initial treatment. Pharmacotherapy of patients with intermittent claudication is aimed at reducing cardiovascular mortality rather than the distance of claudication. All risk factors, such as hypertension and DM, should be strictly controlled. Antiplatelet agents and statins are prescribed to reduce the occurrence of cardiovascular complications.<sup>18th</sup>

Regarding surgical management, it should be noted that it is considered when the conservative approach, which includes lifestyle changes and medications, is not sufficient to relieve symptoms or when arterial obstruction is severe enough to threaten tissue viability. The choice of technique depends on the extent and location of the arterial obstruction.

In angioplasty, a catheter is inserted into the obstructed artery and an inflatable balloon at the end of the catheter is inflated to dilate the obstruction, in many cases a stent (mesh-shaped device) is placed to keep the artery open, preventing recurrence of the obstruction, this approach is minimally invasive and can be performed through a small incision or even percutaneously.



The in-depth implications of stents in the management of PAOD and their repercussions on hemodynamics and blood flow are remarkable. However, just as every procedure requires improving the effectiveness of stents in restoring blood flow, there is a wide range of stent design strategies, such as coated stents, all of which are presented as an attempt to optimize local hemodynamics and facilitate efficient recovery of the affected vessel. We can note that the analysis of the advantages and disadvantages of this approach offers relevant considerations for the management of PAOD through this technique, and provides an in-depth understanding of the impact of stents on blood circulation. However, revascularization with stenting causes arterial trauma and introduces abnormal hemodynamics, initiating complicated biological processes that are harmful to the arterial wall. The interaction between the stent rods, the arterial cells in contact, and the blood flow field created in a stent region, are highly affected by the stent design. Spiral flow is known as a normal physiological feature of arterial circulation and is thought to prevent the development of flow disorders. This secondary flow movement is lost in atheromatous disease, and its reintroduction after endovascular treatment of PAOD has been suggested as a method to induce stabilized and coherent hemodynamics.<sup>23,24</sup>

Vascular bypass is an option in more complex cases, when it is necessary to create a bypass around the obstruction, using a vascular graft to restore normal blood flow. The graft can be an autologous vein (from the patient himself) or a synthetic graft. This procedure is similar to heart bypass surgeries performed on the heart to treat coronary artery disease. For patients with premature PAOD and advanced femoropopliteal disease, bypass surgery decreased the rate of reintervention at 1 year, however, it was associated with increased perioperative morbidity and longer hospital stay compared with endovascular therapy.<sup>26th</sup>

Regarding peripheral revascularization in cases of PAOD, recent analyses have made clear the risk of adverse events in the limbs in patients with PAOD. It can be highlighted that in primary care patients aged  $\geq 65$  years, the rate of peripheral revascularization of the lower limbs increased by 1.5/1000 person-years, while the rate of events was 11/1000 person-years, in individuals with asymptomatic PAOD, an increase of 5.5 times compared to those without a previous diagnosis of PAOD, in patients with symptomatic patients, the rate of revascularization and limb amputation was 32/1000 person-years, a 15-fold increase compared to people without PAOD. The rate of serious adverse events in extremities was observed to be 7.2% in placebo-treated subjects over 3 years of follow-up compared to 3.7% in vorapaxar-treated subjects. Three-quarters of these subjects had an ankle-brachial index  $\leq 0.9$ , while 40% had undergone



previous revascularization. In the placebo group, there was a 14% rate of revascularization and a 2.3% rate of hospitalization for acute limb ischemia.<sup>27th</sup>

The hybrid approach seeks to optimize the benefits of traditional and endovascular surgical interventions, aiming to reduce complications and improve treatment effectiveness. The overall rate of hybrid endovascular revascularization procedures has seen a notable increase, the hybrid procedure has been significantly more used in patients with claudication, while bypass surgery has often been used in patients with tissue loss. The hybrid approach was associated with a lower rate of myocardial infarction and renal complications, shorter length of hospital stay, and higher discharge rate for bypass surgery. There was no significant difference in 30-day mortality. Comparison of outcomes at 1 year suggested that patients in the bypass group were more likely to have improved outpatient status compared to patients in the hybrid approach group. However, the analysis showed no difference in overall survival or amputation-free survival between the two groups. There was no statistical difference in grafting, limb loss, or secondary interventions.<sup>27th</sup>

Amputations may occur, in general they present in extreme cases where the patient did not adhere to the previously mentioned conservative management or, in cases where the surgical approach did not have the expected effect, severe cases in which tissue viability is compromised and other interventions are not effective, amputation may be the only option to prevent the spread of infections.

Among the presentations that were most related to limb amputations in cases of PAOD, the most prevalent was gangrene, an infected wound that does not heal and the development of a 30-day risk prediction scoring system. To analyze the results: after major amputations of the lower limbs, intraoperative deaths are almost nil, the duration of the intervention is < 60 minutes, in at least 50% of the cases in which it is necessary, the average postoperative hospitalization is 8 days. The mortality rate is associated with three predictive variables associated with 30-day mortality: age > 80 years, chronic obstructive pulmonary disease, and hemodialysis. Despite a more aggressive policy regarding peripheral revascularization, better medical management and preoperative optimization, as well as anesthetic improvements. However, no clinical or physiological parameter is really able to reliably predict a poor outcome after amputation due to PAOD.<sup>28th</sup>





## FINAL THOUGHTS

It is important to highlight that conservative management as well as recommendations for lifestyle improvement should be prioritized after the diagnosis of PAOD. In cases where a surgical approach is necessary, the choice of technique will depend on the patient's detailed evaluation, including the location and extent of the obstruction, the presence of underlying medical conditions, and the patient's overall health. In addition, the surgical approach can be combined with other treatment modalities, and with the control of risk factors, to optimize long-term outcomes.

The study pointed to a significant increase in the use of hybrid approaches, especially in femoropopliteal revascularization. This trend suggests a positive adaptation to changes in clinical practice, aiming to improve perioperative outcomes. Hybrid (hybrid) endovascular revascularization has advantages in terms of lower incidence of complications such as myocardial infarction, renal complications, and length of hospital stay when compared to femoropopliteal bypass alone.

While hybrid RSI shows perioperative benefits, it is crucial to consider the long-term implications. The one-year comparison reveals that patients undergoing femoropopliteal bypass have a higher likelihood of improvement in outpatient status. This highlights the need for continuous evaluation to determine the long-term success of each approach. The choice between the clinical approach and the different surgical options should be personalized, taking into account factors such as disease severity, comorbidities, and the patient's risk profile. The hybrid approach may be favored in high-risk patients due to its perioperative advantages.

The analysis of graft survival and patency highlights the importance of long-term follow-up to assess the efficacy and durability of the interventions performed. Ongoing follow-up is essential for adjustments to the treatment plan if necessary.

The vascular surgeon plays a crucial role in deciding and executing the most appropriate procedure for each case. In summary, the evolution in clinical management and surgical approaches to PAOD represents a significant advance, providing safe and effective options for patients. The hybrid approach, in particular, emerges as a promising strategy, especially in high-risk patients. However, individualized evaluation and long-term follow-up remain critical to optimize clinical and surgical outcomes.



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