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ACUTE CORONARY SYNDROME AND PERIPHERAL ARTERY DISEASE – A HIGH-RISK ASSOCIATION WITH PROGNOSTIC IMPACT

DOCTORAL THESIS ABSTRACT

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INTRODUCTION

Peripheral Artery Disease of the Lower Limbs, also Known as Peripheral Obliterative Arteriopathy, Refers to Atherosclerotic Conditions of the Arteries Supplying the Limbs, from the Aortoiliac Segments to the Plantar Arteries. The most common symptom is lower limb pain that occurs during walking and improves with rest, known as intermittent claudication. Depending on the severity of the disease, some patients may experience pain even at rest. Paradoxically, up to 50% of these patients either have no symptoms or exhibit atypical symptoms in the lower limbs [1].

More than 200 million adults suffer from peripheral artery disease, significantly increasing their risk of major cardiovascular events such as ischemic coronary artery disease, stroke, and limb amputation. Globally, PAD remains underdiagnosed and undertreated, primarily due to insufficient awareness of the disease [2].

Although this condition has a major impact on clinical prognosis, physical function, and activity levels, it has been less studied and recognized compared to other atherosclerotic diseases, such as myocardial infarction. In recent years, scientific evidence regarding the significant association between PAD and mortality has become increasingly consistent, highlighting its role as a risk factor for myocardial infarction and stroke. Moreover, PAD can lead to severe complications, such as acute limb ischemia and major amputations.

While atherosclerotic diseases share pathogenic mechanisms, their causes are not identical, and the appropriate diagnosis and treatment of PAD remain major challenges in medicine. Clinically, PAD and coronary artery disease (CAD) present numerous similarities, sharing common risk factors. Among affected patients, dyslipidemia and type II diabetes mellitus are significant comorbidities. Multiple studies have demonstrated the high prevalence of concomitant CAD and PAD, underscoring the importance of recognizing and treating these conditions together [3]. To improve prognosis and quality of life in this growing and undertreated population, a better understanding of the definition, diagnosis, clinical manifestations, and complications of peripheral artery disease is essential.

Coronary atherosclerosis frequently manifests as acute coronary syndromes (ACS), in which thrombosis is triggered by the rupture or erosion of the fibrous cap of atherosclerotic plaques. Typically, ruptured plaques exhibit large necrotic cores and thin, highly inflammatory fibrous caps. Regarding peripheral artery disease, regardless of the severity of atherosclerosis, thrombosis is the main manifestation. In peripheral arteries with

significant stenosis, approximately 75% become occluded due to thrombosis, and two-thirds of them present thrombi in the context of non-significant atherosclerosis. Furthermore, in patients without typical coronary lesions, critical limb ischemia can be explained by the presence of local obliterative thrombosis or distant embolic phenomena.

Based on these aspects and the necessity of further exploring the relationship between peripheral artery disease and acute coronary syndromes, we hypothesized that the presence of PAD significantly influences left ventricular systolic function and contributes to the onset of acute heart failure (AHF) in the context of ACS.

The first prospective study in this thesis aimed to conduct a detailed analysis of the impact of PAD on left ventricular ejection fraction (LVEF) and the risk of acute heart failure in ACS patients. The study sought to assess the incidence and severity of left ventricular dysfunction based on the presence of PAD, considering that nearly 50% of PAD patients also have concomitant coronary artery disease.

In this retrospective case-control study, 100 patients hospitalized with ACS were analyzed (mean age = 61.03 years, 80% male), divided into two groups: a group of ACS patients with PAD (32 patients, of whom 74% had STEMI, 10% had NSTEMI, and 16% had NSTEACS) and a control group without PAD (68 patients).

The study results highlighted that PAD has a significantly negative impact on patients with non-ST elevation myocardial infarction (NSTEMI), who experienced an average decline of 19.3% in left ventricular ejection fraction compared to patients without PAD ($p = 0.003$). Additionally, patients in the PAD group were significantly more frequently associated with Killip Class IV ($p = 0.049$), indicating a more severe clinical status. These findings emphasize the importance of early recognition of PAD in ACS patients, as they have a higher risk of acute heart failure and an increased incidence of cardiovascular risk factors such as diabetes mellitus, hypertension, dyslipidemia, and active smoking. Moreover, a detailed analysis of patients with unstable angina (UA) and PAD revealed that they tend to have an apparently preserved ejection fraction (>55%) but exhibit a more unstable clinical status characterized by acute pulmonary edema and cardiogenic shock. This discrepancy may be explained by the high prevalence of heart failure with preserved ejection fraction (HFpEF) among PAD patients.

Through this study, we aim to contribute to a better understanding of the impact of PAD on ACS patient outcomes and to highlight the necessity of personalized therapeutic strategies for this high-risk cardiovascular patient category.

In the second case study, we aimed to evaluate the impact of peripheral artery disease on the prognosis of patients hospitalized with acute coronary syndrome. Given the high prevalence of coronary artery disease in PAD patients, we investigated the extent to which this association influences the severity of coronary lesions and the necessity for complete revascularization during hospitalization. The severity of coronary artery disease was assessed using the SYNTAX score, and revascularization procedures were analyzed based on the need for complete revascularization and the involvement of the left main coronary artery.

Study results indicated that ACS patients with PAD had an average SYNTAX score 6.8 points higher than those without PAD ($p=0.034$), suggesting more severe coronary involvement. In patients with UA and PAD, the SYNTAX score was 12.7 points higher ($p=0.008$), reflecting a higher cardiovascular risk and increased complexity of coronary lesions. Additionally, ACS patients with PAD required complete revascularization more frequently, with significant involvement of the left anterior descending artery and the left main coronary artery, which could influence long-term prognosis.

These findings highlight the necessity of a more aggressive therapeutic approach in patients with PAD and ACS, considering their increased risk of major cardiovascular events and the need for personalized revascularization strategies. The study contributes to a better understanding of the relationship between PAD and coronary artery disease severity, providing relevant data for optimizing the treatment of these high-risk cardiovascular patients.

Although the studies included in this doctoral thesis provide important insights into the impact of peripheral artery disease on acute coronary syndrome, they present certain methodological and clinical limitations that must be considered. These limitations may affect the interpretation and applicability of the results in clinical practice, emphasizing the need for additional studies to validate and expand the obtained conclusions.

Both studies were conducted on a relatively small sample of patients (100 participants), which may limit the generalization of results at a population level. One of the main limitations is the lack of long-term follow-up of patients, preventing the assessment of the evolution of ejection fraction and heart failure over time. Although the study highlights a negative impact of PAD on left ventricular function, it is not possible to determine with certainty whether this effect persists or worsens over time. Additionally, there is no long-term mortality data, hospital readmissions for heart failure, or recurrence of major cardiovascular events (MACE), which are essential factors in characterizing the overall impact of PAD on ACS patients.

Despite these limitations, the studies provide valuable information on the relationship between PAD and ACS severity, demonstrating that patients with this association have a higher cardiovascular risk and require personalized therapeutic strategies. To validate these results, prospective, multicenter studies with larger patient samples and long-term follow-up are necessary.

THEORETICAL FOUNDATIONS AND CONTEXT OF THE PROBLEM

Peripheral Artery Disease and Coronary Artery Disease Are Two Manifestations of Systemic Atherosclerosis, Characterized by the Narrowing or Occlusion of Arteries, Generally Due to the Accumulation of Atherosclerotic Plaques. PAD predominantly affects the arteries of the lower limbs, causing claudication due to reduced distal blood flow, while coronary artery disease affects the coronary arteries, increasing the risk of angina pectoris and myocardial infarction.

Peripheral artery disease has significant clinical importance as it is associated not only with local symptoms that affect patient mobility and quality of life but also with a major cardiovascular risk, including myocardial infarction, stroke, and the development of abdominal aortic aneurysms, necessitating appropriate diagnostic and treatment strategies [4,5]. PAD significantly impacts patients' quality of life by limiting exercise capacity and causing ischemic pain. Intermittent claudication, characterized by lower limb pain during walking, is one of the most common manifestations. As the disease progresses, patients may develop critical limb ischemia, with resting pain, ulcerations, and a risk of amputation. Reduced mobility and decreased physical activity also create a vicious cycle of physical deconditioning and metabolic deterioration. Studies indicate that PAD patients have a 2- to 4-fold increased risk of myocardial infarction and stroke compared to the general population. Furthermore, nearly 50% of PAD patients also have concomitant coronary artery disease [6], highlighting its systemic nature and the need for extensive cardiovascular screening.

One of the greatest clinical challenges is the late diagnosis of PAD, as many patients remain asymptomatic or develop nonspecific symptoms. Data suggest that up to 50% of PAD patients do not experience intermittent claudication, leading to underdiagnosis and delayed treatment. Additionally, there is a gap in optimal treatment, as many PAD patients do not receive appropriate therapy with antiplatelet agents and statins, which are essential for reducing cardiovascular risk. Given its systemic impact, PAD requires a multidisciplinary approach involving cardiologists, vascular surgeons, diabetes specialists, and rehabilitation medicine experts. The goal of treatment is not only to alleviate local symptoms but also to reduce overall cardiovascular risk through aggressive risk factor control, optimal pharmacological therapy, and, in severe cases, revascularization (drug-

coated balloon angioplasty, stent placement, or arterial bypass surgery).

The importance of this research stems from the need to better understand how PAD influences left ventricular ejection fraction and the risk of acute heart failure in ACS patients. Early identification of these high-risk patients is essential for optimizing therapeutic strategies and reducing associated morbidity and mortality. Another key aspect of our study is the evaluation of prognostic differences based on PAD severity and its impact on left ventricular function. Furthermore, the study aims to provide a detailed analysis of the relationship between peripheral artery disease and coronary artery disease, exploring the overlap of these pathologies and their effects on the complexity and progression of acute coronary artery disease.

HYPOTHESIS AND RESEARCH OBJECTIVES

Study 1: Assessment of the Impact of Peripheral Artery Disease on Left Ventricular Function and the Risk of Acute Heart Failure in Patients with Acute Coronary Syndrome. Hypothesis: Peripheral artery disease represents a significant negative prognostic factor, being associated with a reduction in left ventricular function and a substantial increase in the risk of acute heart failure in patients with acute coronary syndrome.

Primary Objective: To evaluate the relationship between the presence of peripheral artery disease and changes in left ventricular function, quantified by the left ventricular ejection fraction (LVEF), measured echocardiographically during hospitalization and in the short-term follow-up period. Additionally, to quantify and analyze the incidence of acute heart failure in ACS patients with PAD compared to those without PAD.

Secondary Objectives: Identification of clinical and paraclinical factors (age, comorbidities, serum biomarkers) associated with left ventricular function deterioration and the risk of acute heart failure. Investigation of the relationship between PAD severity, measured by the ankle-brachial index and the prognosis of ACS patients during short- and medium-term follow-up.

Study 2: Influence of Peripheral Artery Disease on the Complexity of Coronary Artery Disease Quantified by the SYNTAX Score in Patients with Acute Coronary Syndrome.

Working Hypothesis: The presence of peripheral artery disease in patients with acute coronary syndrome is associated with a higher SYNTAX score, implying increased coronary artery disease complexity, with direct implications for interventional management and cardiovascular prognosis.

Primary Objective: To investigate the influence of peripheral artery disease on the SYNTAX score, which assesses the severity and complexity of coronary artery disease in patients with acute coronary syndrome. To evaluate how the presence of PAD affects interventional therapeutic decisions and the prognosis of ACS patients.

Secondary Objectives: Analysis of clinical and paraclinical factors associated with coronary artery disease complexity, measured by the SYNTAX score in patients with PAD and ACS. Assessment of the impact of peripheral artery disease on hospitalization duration, incidence of major cardiovascular events (reintervention, ischemic stroke), and

cardiovascular mortality during short- and medium-term follow-up.

Comparative analysis of clinical and angiographic outcomes of coronary revascularization in patients with and without PAD to optimize therapeutic approaches and reduce complications.

RESEARCH METHODOLOGY

The research methodology used in this doctoral thesis consisted of conducting two prospective studies.

A sample of 100 patients hospitalized with acute coronary syndromes was used. The patients were divided into two groups: one group consisting of 32 patients diagnosed with both peripheral artery disease and ACS, and a control group comprising 68 patients with ACS but without PAD. The diagnosis of PAD was established based on clinical and imaging criteria, while the presence of ACS was confirmed according to the current guidelines of the European Society of Cardiology. Within the study, the left ventricular ejection fraction, the severity of acute heart failure (Killip classification), and cardiovascular risk factors were analyzed.

The second study assessed the severity of coronary artery disease and the need for complete revascularization in patients with ACS and PAD compared to patients with ACS without PAD. To this end, the severity of coronary artery disease was quantified using the SYNTAX score. Coronary angiographies performed during hospitalization were retrospectively analyzed, and the data included an assessment of the involvement of the left anterior descending artery and the left main coronary artery, as well as the necessity for complete revascularization.

The statistical methods used included the Student's t-test and chi-square test for comparing numerical and categorical parameters between groups. The statistical significance threshold was set at $p<0.05$. The methodological limitations of the studies included the small sample size and the lack of longitudinal follow-up, which were considered when interpreting the results.

SUMMARY OF THE CHAPTERS FROM THE SPECIAL SECTION

In Chapter 3 of the thesis, the impact of peripheral artery disease on patients hospitalized with acute coronary syndromes was analyzed. The prospective retrospective study included 100 patients, divided into two distinct groups: 32 patients diagnosed with both ACS and PAD and 68 patients diagnosed only with ACS. The diagnosis of peripheral artery disease was established based on current clinical and imaging criteria, including the ankle-brachial index and, in selected cases, using Doppler ultrasound or angiography.

The primary objective was to assess the impact of peripheral artery disease on left ventricular ejection fraction and the risk of acute heart failure. The results showed that patients with non-ST elevation myocardial infarction (NSTEMI), unstable angina, and peripheral artery disease had a significant reduction in LVEF, with an average decrease of 19.3% compared to patients without peripheral artery disease ($p=0.003$). Additionally, patients with PAD more frequently presented with severe acute heart failure (Killip Class IV, $p=0.049$), reflecting a more critical clinical condition.

Patients with unstable angina and PAD, despite having an apparently preserved ejection fraction (>55%), exhibited increased clinical instability, with severe episodes such as acute pulmonary edema and cardiogenic shock. This finding suggests that PAD patients are predisposed to a more severe form of acute heart failure.

The analysis of cardiovascular risk factors revealed that PAD patients had higher prevalence rates of type II diabetes mellitus, hypertension, dyslipidemia, and active smoking compared to patients without PAD, indicating the necessity for a multidisciplinary and personalized therapeutic approach for this patient category.

Chapter 4 focused on assessing the severity of coronary artery disease and the need for complete revascularization in patients diagnosed with acute coronary syndromes and concomitant peripheral artery disease. The severity of coronary artery disease was quantified using the SYNTAX score, a validated tool used to evaluate the complexity of coronary lesions.

The methodology included a retrospective analysis of coronary angiographies performed during hospitalization for ACS. The results indicated that patients with ACS and PAD had a significantly higher SYNTAX score (6.8 points higher; $p=0.034$) compared to those without PAD, reflecting the increased severity of coronary involvement. In the

subgroup of patients with unstable angina and PAD, the difference in SYNTAX score was even more pronounced (12.7 points higher, p=0.008).

PAD patients frequently required complete revascularization and had significant involvement of the left anterior descending artery and left main coronary artery, highlighting the complexity of coronary artery disease in this group. This necessitated more aggressive invasive therapeutic strategies and a detailed angiographic evaluation.

The major clinical implications include the necessity for integrated and personalized therapeutic strategies for patients with PAD and ACS, considering their high cardiovascular risk and the greater complexity of coronary artery disease. Early recognition and appropriate therapeutic interventions are essential for improving prognosis and reducing major cardiovascular complications.

The study's limitations included the small sample size and the lack of long-term follow-up, which may limit the generalizability of the results. To validate and expand the presented conclusions, future prospective, multicenter studies with larger patient samples and extended monitoring periods are required.

CONCLUSIONS

The first study revealed that the presence of peripheral artery disease in patients with acute coronary syndrome, particularly in those with NSTEMI, is associated with a significant reduction in left ventricular ejection fraction . Patients with NSTEMI and an ABI below 0.9 showed an average LVEF reduction of approximately 19.3% ($p = 0.003$) compared to those without PAD. Additionally, these patients had a higher probability of being classified as Killip IV ($p = 0.049$), indicating an increased risk of severe heart failure and an unfavorable clinical evolution. The study also found that patients with unstable angina and PAD tended to have an apparently preserved LVEF (>55%) but exhibited increased clinical instability, including acute pulmonary edema and cardiogenic shock.

Further analyses indicated that patients with NSTEMI and PAD were more likely to have an LVEF above 55%, with a p-value of 0.016, while patients with unstable angina and an ABI below 0.9 had, on average, an LVEF that was 5.7% higher than others ($p=0.056$) [7]. This phenomenon may be explained by the development of more efficient coronary collateral circulation in elderly patients, which could reduce infarct size and preserve systolic function.

Additionally, the study found that PAD patients had elevated levels of traditional cardiovascular risk factors such as type II diabetes mellitus, hypertension, and dyslipidemia compared to the control group. Moreover, it was observed that patients with STEMI and PAD had HEART scores that were approximately 1.06 points higher ($p=0.002$), suggesting an increased overall cardiovascular risk. In contrast, patients with unstable angina and PAD had lower HEART scores, with an average reduction of 0.96 points ($p=0.023$), suggesting a lower immediate risk upon hospitalization.

Thus, the presence of PAD represents a significant risk factor associated with more severe clinical impairment, requiring an intensive and personalized therapeutic approach to improve the prognosis of patients with acute coronary syndromes.

The second study analyzed the impact of peripheral artery disease on the anatomical complexity and severity of coronary artery disease in patients with acute coronary syndromes. Using the SYNTAX score, it was found that patients with ACS and an ABI below 0.9 had significantly greater complexity of coronary artery disease compared to patients without PAD (an average increase of 6.8 points) [8]. This complexity was even more pronounced in patients with unstable angina, with an average SYNTAX score increase of 12.7 points compared to those without PAD. The likelihood of patients with unstable angina

and PAD having a SYNTAX score below 22 was only 18%, compared to 63% in patients without PAD and unstable angina, emphasizing the severity of coronary involvement in this subgroup.

Additionally, NSTEMI patients had significantly higher SYNTAX scores compared to STEMI patients, reflecting more extensive and severe coronary artery disease. It was observed that patients with PAD and ACS received, on average, 22.1 mL more contrast agent than those without PAD, and STEMI patients with PAD had significantly higher cumulative radiation exposure (35.9 mGy/cm²). These findings suggest that the presence of PAD is associated with additional procedural risks during percutaneous coronary interventions, including increased exposure to contrast agents and radiation.

The study also highlighted that PAD patients more frequently required complete revascularization and had severe and frequent involvement of the left main coronary artery and the left anterior descending artery, underscoring the need for a complex and aggressive therapeutic approach.

The results emphasize the role of the ABI as a predictor of coronary artery disease complexity and the importance of adopting special measures to reduce the procedural risks associated with this patient category. These observations are supported by previous studies, such as those conducted by Korkmaz [9] and Aykan [10], which demonstrated significant correlations between ABI and the SYNTAX score, as well as the importance of ABI in predicting coronary anatomical complexity.

In conclusion, both studies demonstrate that patients with peripheral artery disease and acute coronary syndromes represent a high-risk category, requiring personalized therapeutic approaches, increased attention in clinical and interventional management, and detailed risk assessments of procedures to improve prognosis and reduce major cardiovascular complications.

PERSONAL CONTRIBUTIONS

This doctoral thesis brings multiple original contributions to the fields of cardiology and internal medicine. The study demonstrated that patients with peripheral artery disease have a significantly higher SYNTAX score, emphasizing that atherosclerotic involvement is more extensive in these patients. This conclusion has major clinical implications, suggesting the need for a more rigorous assessment and a more aggressive therapeutic approach.

The research results showed that patients with peripheral artery disease more frequently require complete revascularization, particularly for left main coronary artery lesions or lesions in the left anterior descending artery. This finding can guide clinicians in selecting optimal treatment strategies. The study demonstrated that patients with peripheral artery disease have a higher risk of mortality and reintervention, underscoring the importance of early identification of this condition and the implementation of appropriate preventive measures.

Patients with peripheral artery disease received significantly higher doses of contrast agents and were exposed to greater cumulative radiation, highlighting the need to optimize imaging and interventional strategies to reduce these risks. The study also revealed specific differences in the severity of coronary artery disease among ACS subgroups, demonstrating that patients with STEMI and peripheral artery disease exhibit the most severe forms of coronary artery disease.

An important contribution of this thesis is the analysis of the impact of PAD on left ventricular ejection fraction and the risk of acute heart failure in patients with acute coronary syndrome. The study results indicate that patients with peripheral artery disease had significantly lower ejection fractions compared to those without PAD, highlighting the negative influence of peripheral arterial impairment on myocardial function. Moreover, a correlation was observed between the presence of peripheral artery disease and an increased risk of acute heart failure, suggesting that these patients require closer monitoring and appropriate cardioprotective therapies.

Through these contributions, this doctoral thesis provides significant insights into the relationship between peripheral artery disease and acute coronary syndrome, offering new perspectives on the optimal management of these high-risk cardiovascular patients.

The study suggests the need for larger prospective studies to evaluate the impact of personalized treatments in patients with PAD and ACS, as well as the effectiveness of new strategies to reduce contrast and radiation exposure. These findings could contribute to the development of updated clinical guidelines for the integrated management of patients with multi-territorial atherosclerotic disease.

The advantages of using the ankle-brachial index in the evaluation of patients with acute coronary syndrome are numerous. ABI is a simple, non-invasive, and cost-effective method, allowing its widespread use in clinical practice. Determining ABI can improve risk stratification and guide therapeutic decisions, contributing to the early identification of patients with peripheral artery disease and severe coronary involvement. Additionally, ABI assessment can enable more efficient allocation of medical resources, directing high-risk patients toward further investigations and personalized therapeutic strategies.

Regarding imaging and interventional strategies, this study highlighted the need for tailored approaches for patients with peripheral artery disease. Although these strategies may involve higher initial costs due to the use of advanced technologies, the long-term benefits may justify these investments by reducing complications and optimizing patient prognosis. Complete revascularization and close monitoring of PAD patients can help reduce hospital readmission rates and mortality, with a favorable economic impact on the healthcare system.

On the other hand, there are significant disadvantages associated with the use of ABI and intensive imaging strategies in managing ACS patients. First, standardized protocols integrating ABI into revascularization decision-making algorithms are still lacking, limiting its widespread clinical applicability. Second, the need for advanced imaging strategies and increased exposure to contrast agents and radiation in PAD patients entails additional risks and higher costs for the medical system. Repeated contrast exposure may lead to contrast-induced nephropathy, while intensive fluoroscopy use may increase the risk of radiation-related complications.

Another technical and economic disadvantage relates to the need for broader screening to identify patients with a low ABI. Implementing screening programs may require additional resources and training of medical personnel for accurate ABI measurement. Furthermore, limited access to advanced imaging technologies in some medical centers may be a barrier to the optimal application of personalized revascularization strategies in PAD patients.

Regarding unresolved issues and future research directions, while this study provides clear evidence of the relationship between peripheral artery disease and the severity of coronary artery disease, many aspects still require further investigation. An important limitation of the study is the sample size and the need for multicenter studies to confirm these findings in a broader setting. It remains unclear whether a differentiated treatment strategy based on ABI could improve patient prognosis, and this aspect should be explored in future studies.

Another unresolved issue is the optimal use of ABI screening in clinical practice. Although this method is simple and non-invasive, there are no clear recommendations regarding the best timing for ABI evaluation in acute coronary syndrome patients. Additionally, it is not yet well established whether integrating ABI into risk stratification scores could improve therapeutic decision-making.

Regarding contrast and radiation exposure, studies are needed to identify optimized protocols to reduce these risks in patients with ABI < 0.9. Another aspect requiring further research is the link between peripheral artery disease and heart failure in patients with acute coronary syndrome. Although this thesis has highlighted an association between ABI < 0.9 and reduced ejection fraction, the exact pathophysiological mechanisms remain incompletely understood. Future studies could explore whether early therapeutic interventions for PAD might improve ventricular function in these patients.

Through these contributions, this thesis provides a new perspective on the relationship between PAD and the severity of coronary artery disease, emphasizing the need for an integrated approach in managing acute coronary syndrome patients. The findings suggest that patients with ABI < 0.9 require closer monitoring, more aggressive therapeutic strategies, and optimization of contrast and radiation exposure. These discoveries could serve as the foundation for future clinical guidelines aimed at improving the prognosis of patients with multi-territorial atherosclerotic disease.

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1. **Flavius-Alexandru Gherasie**, Mihaela-Roxana Popescu *, Daniela Bartoș, Acute Coronary Syndrome: Disparities of Pathophysiology and Mortality with and without Peripheral Artery Disease, Journal of Personalized Medicine, 2023, 13(6), 944. https://doi.org/10.3390/jpm13060944;https://www.mdpi.com/2075-4426/13/6/944;Factor Impact 3.0;
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