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# Peripheral Arterial Disease in Patients with Atrial Fibrillation

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#### **ABSTRACT**

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#### Mini Review

Peripheral Arterial Disease (PAD) is defined as a systemic atherosclerotic disease, which occurs due to narrowing and obstruction of major systemic arteries other than coronary arteries and aorta. It affects 200 million individuals worldwide and is independent risk factor for total mortality and incident cardiovascular or cerebrovascular events [1]. Da-ta of Rotterdam study present that only 10% of 55-59 years old participants had PAD and 60% subjects in age group >85 years was diagnosed with this condition.

According to the National Health and Nutrition Examination Survey 1999-2000 major risk factors for PAD include arterial hypertension, diabetes, hypercholesterolemia, smoking, obesity. Over 95% of patients with peripheral arterial disease has one of these risk factors and over 70% has two major risk factors. Some studies suggest that chronic renal failure may influence manifestation of PAD. Collaborative meta-analysis of international cohorts made by Matsushita et al. showed that even mild-to-moderate chronic kidney disease increases risk of incident peripheral artery disease [2].

Increased inflammatory markers such as C-Reactive Protein (CRP) have an impact on PAD. CRP demonstrated a statistically significant correlation of risk for PAD compared with patients without PAD [3-5]. Classical clinical manifestation of low extremities PAD include aching pain especially in the calves which occurs during activity and reliefs by rest (intermittent claudication), poikilothermic (cold sensation), pallor of the limb and ulceration. Most of the cases patients are associating these signs with other earlier diagnosed disease such as diabetes, arthritis, etc. In the PIPETTE study 33% of participants with severe symptoms of

intermittent claudication that warranted subsequent endovascular intervention had not previously presented to their general practice [3]. Up to 50% of patients with PAD has no symptoms and this group is most under-recognised and under-treated. This is one of the reasons why PAD is diagnosed in severe stages with high mortality risk.

Early diagnosis of PAD is important to prevent cardiovascular complications. Ac-cording to NHANES mortality from cardiovascular events among patients diagnosed with PAD was 29.2% [4]. Simple, non-invasive, fast and cheap tool to diagnose this condition is the Ankle-Brachial Index (ABI). The measurement of blood pressure at the ankle was proposed as a test for PAD as early as 1950 and led to the development of the Ankle-Brachial Index (ABI) [1]. ABI is defined as the ratio between systolic blood pressure at the ankle and in the arm. Measurements may be obtained using Doppler ultrasound or oscillometric sphygmomanometry. An ABI of <0.9 is considered as abnormal and is associated with symptomatic and asymptomatic forms of PAD and higher risk of cardiovascular events. According to 2017 ECS guidelines on the diagnosis and treatment of peripheral arterial disease an ABI < 0.90 is associated with 2- to 3-fold increased risk of total and cardiovascular death.

American Heart Association recommends determining anklebrachial index in the following cases: adults ≥65 years old, adults ≥50 years old with a history of smoking or diabetes, and adults of any age with exertional leg symptoms or non-healing wounds. European Society of Cardiology suggests considering screening with ABI in patients with Coronary Artery Disease (CAD).

ARTPER cohort study showed that at 9 years 20% of patients with low ABI had ma-jor cardiovascular events such as myocardial

infarction, ischaemic stroke and vascular mortality. Patients with borderline ABI (0.90-0.99) should be considered also as a high-risk group and further diagnostic tests should be made [6]. The Multi-Ethnic Study of Atherosclerosis (6570 participants) identified that patient with PAD and low ABI (< 0.90) had twice risk for the development of atrial fibrillation or stroke [7]. Peripheral arterial disease is common in patients with Atrial Fibrillation (AF), but the association between these two conditions are not completely understood. Both diseases share risk factors such as diabetes, arterial hypertension, hypercholesterolemia and are associated with increased levels of inflammation and platelet-mediated thrombosis [7].

Cohort study (5143 participants) reporter that incident rate of AF significantly higher in group with PAD compared with patients without PAD. Risk of AF increases 6% with each 0.1 decreasing of ABI [8,9]. Other large cohort study (582,635 subjects) resulted PAD as independent risk factor for AF - for 10 years follow-up period events of AF was significantly higher for participants with PAD, they had 1.286 times higher incident rate to develop AF [10]. In the ARAPACIS study 21% of patients with Non-Valvular Atrial Fibrillation (NVAF) had ABI <=0.90, which indicates that NVAF is associated with systemic atherosclerosis, including PAD [9].

In other hand several studies suggest that increased heart rate in AF patients has major impact for arterial stiffness and may affect measurements of ABI [11,12]. In general, the ankle-brachial index determines how well blood is slowing in body. During atrial fibrillation peripheral pulse wave may not be registered correctly, which can lead to an incorrect ABI result. We know that risk factors of AF such as diabetes, hypertension are associated with inflammation. Atherosclerosis is also a chronic inflammatory disease, so this condition may result falsely high ratio due to the presence of incompressible calcified blood vessels.

E. Mašanauskienė et al. [13] suggested an alternative non-invasive method to diagnose PAD - Impedance Plethysmography (IP). Extremities impedance results about peripheral vascular response to the quantity and velocity of circulating blood and peripheral vascular resistance. Significant correlation were found between ABI and IP parameter Crest Time (CT). They found CT sensitivity of 73% and specificity of 95%. Dachun Xu et al. [14] reported specificity (83.3-99.0%) and accuracy (72.1-89.2%) of ABI by diagnosing  $\geq$  50% stenosis, but sensitivity ranged from15 to 79% especially elderly participants or subjects with diabetes.

Considering to all results impedance plethysmography could be used to diagnose peripheral circulation disorders, especially in patients with high risk of atherosclerosis and other conditions such as atrial fibrillation which may lead to falsely ABI results.

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