An Ignored Disease of Cardiovascular System: Peripheral Arterial Disease

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Abstract

Peripheral arterial disease (PAD) is the chronic and progressive deterioration of lower extremity arterial blood flow due to systemic atherosclerosis. Currently, PAD is considered not only a disorder of lower extremity circulation and but also a predictorofincreased mortality and morbidity. In prevalence surveys conducted in Turkey, the frequencyof PAD was found up to 20-30%, increasing with advancing age. The diagnosis of PAD can easily be made by the ankle brachial index measurement. The incidence of coronary artery disease and congestive heart failure is higherin individuals with PAD. In addition, in patients with coronary artery disease or congestive heart failure, cardiovascular mortality and all - cause mortality increases in the presence of PAD. In conclusion, PAD is a systemic disease and should be treated systematically and effectively in addition to interventional therapies.

Keywords: Peripheral arterial disease; Coronary artery disease; Heart failure; Ankle brachial index; Drug therapy

Introduction

Peripheral arterial disease (PAD) is defined as the chronic and progressive deterioration of the lower extremity arterial blood circulation due to systemic atherosclerosis. Today, PAD constitutes one of the four main categories of cardiovascular disease (CVD) along with coronary heart disease (CHD), cerebrovascular disease, and aorta atherosclerosis/aneurysm [1]. This classification was first described in the National Cholesterol Education Program (NCEP) Adult Treatment Panel III-ATPIII guide and is still relevant [1]. PAD is associated with increased all-cause mortality, cardiovascular mortality and other cardiovascular outcomes [2]. In other words, no difference exists between PAD diagnosed individuals and individuals who have had CHD or cerebrovascular disease in terms of clinical outcomes.

Epidemiology

Among the diseases under the definition CVD, PAD is the most frequent one across different populations. In the first ever survey conducted to explore the prevalence of PAD among Turkish adults and elderly, the frequency of PAD was 20% among individuals aged 50-69 years with at least one cardiovascular risk factor [3]. The study found 30% of PAD among older adults aged 70 years or older, irrespective of risk factors. In a study conducted in the USA with a similar design, overall frequency of PAD was 29% [4]. On the other hand, findings have also been obtained that lower prevalence of PAD was found in outpatient practice of internal medicine [5]. With a very low prevalence in young people [6], the prevalence of PAD increases linearly with age after the fourth decade. The US National Health and Nutrition Examination Survey (NHANES) reported a 0.9% prevalence of PAD between 40 to 49 years of age, whereas 2.5%, 4.7%, and 14.5% were calculated for 50 to 59, 60 to 69, and 70 years and over, respectively, with an average prevalence of 4.3% over 40 years of age [7].

Diagnosis

Angiographic methods are the gold standard for PAD diagnosis [8]. Doppler ultrasonography can also be used for diagnosis, providing additional benefits prior to surgical interventions [9]. The Edinburgh claudication questionnaire not only displays lower sensitivity, but also may vary depending on the procedure selection [10,11]. Today, the most preferred diagnostic method is measurement of the ABI [10,12-14]. While, correct calculation of the index value is seriously important [15], a low ABI value (≤0.9) is not only diagnostic for lower extremity occlusive disease but also a marker of systemic atherosclerosis [16-18]. As in the case of diabetes mellitus, the

diagnostic accuracy of the ABI testing is falsely reduced due to calcinosis on the arterial wall [19]. In any case, ABI is a highly reliable, noninvasive diagnostic method to detect PAD, allowing categorization of the severity of the occlusion [20,21].

PAD and CHD

In patients with CHD, diagnosis of PAD causes significant increases in the frequency of new cardiovascular events and all-cause mortality compared to those without PAD [1]. The incidence of atherosclerosis in coronary arteries is also increased in the presence of PAD [22,23]. Currently, screening for CHD is recommended in individuals with the diagnosis of PAD [24]. However, even in the presence of PAD alone, intensive treatment is required to reduce the risk of atherosclerotic events [1]. There is no clear recommendation to screen for PAD in asymptomatic patients with CHD which is already a major type of CVD with established prevention and treatment goals. In the presence of PAD, it is suggested that screening for concomitant CHD may be beneficial in reducing the risk of coronary ischemic events and death by correctly and early defining the patients who are true candidates of revascularization treatment [25]. However, it has not yet been proven whether such an assumption is met in the clinical practice.

PAD and CHF

Although there are many common risk factors between CHF and PAD, a few studies could identify a relationship between them. A meta-analysis of 11,300 patients showed 7,9%(5,3-13,9%) prevalence of CHF in patients with PAD, while the expected CHF frequency in the community was 4.1% (3.7-4.5%) according to the NHANES database [26]. Accordingly, the relative risk for CHF was 1.9 (1.35-3.1, p<0.001) times higher in patients with PAD and it was estimated that if 13 (7-19) subjects with PAD were screened, one CHF could be identified [26]. Studies on clinical significance of this association have shown that PAD causes worsening in advanced stages of CHF. In the HF-ACTION trial in which the effect of supervised exercise was investigated in addition to standard treatment options for patients with CHF, patients with PAD were less likely to benefit from cardiopulmonary exercise program and PAD was an independent risk factor for all-cause mortality and hospitalizations in patients with CHF [HR (95% CI); 1.31 (1.06-1.62), p=0.011] [27]. Although this study demonstrated limited benefit of exercise in patients with CHF having PAD, supervised exercise therapy is recommended with class IA evidence, without distinction of PAD patients with presence or absence of claudication, with or without CHF [25]. In conclusion, it may be useful to screen individuals with PAD for heart failure due to approximately 2-fold increase in its frequency and higher mortality in patients with CHF having PAD.

Medical Treatment in PAD

All patients with PAD should have antiplatelet and statin treatment if there is no contraindication. Furthermore, in the presence of hypertension and or diabetes mellitus as additional risk factors, treatment should be tailored to the patient. In addition to medical treatment, smoking cessation should be a part of management, along with effective exercise programs.

Statins

In individuals diagnosed with PAD, statin therapy reduced major adverse cardiac events [28-30], limb-related adverse events (worsening of claudication, critical leg ischemia, revascularization and amputation) [27,29,31], limb loss, and mortality after revascularization [30,32-35]. Furthermore, statin therapy increased the total / painless walking distance in patients with PAD [30,33].

Antiplatelet therapy

The use of aspirin alone (75-325mg/day) or clopidogrel alone (75mg/day) in the presence of symptomatic PAD is recommended to reduce the risk of MI, stroke, and vascular death [34-37]. As an expert opinion (Class IIa) [25] using antiplatelet therapy is reasonable in asymptomatic patients with ABI detected PAD, although there is no sufficient data regarding the use of antiplatelet medications to reduce the risk of MI, stroke and vascular death.

Cilostazol and/or Pentoxyfiline

While improvement in walking distance has been previously shown with cilostazol treatment previously [38], a meta-analysis of studies with pentoxifylline treatment did not show any benefit [39]. Therefore, the use of pentoxifylline for this purpose should be decided on a patient-based approach. Use of cilostazol to reduce symptoms and increase walking distance in patients with PAD having claudication is considered an effective treatment option [25].

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