

Tobacco Education: Reduced Risk for Peripheral Artery Disease

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ABSTRACT

Peripheral arterial (vascular) disease (PAD/PVD) in its association with significant mortality and morbidity rates has become a significant public health concern. One of the most influential risk factors for PAD is tobacco use, which carries a 3-4-fold increased risk for PAD often presenting as severe disease. The diagnosis of PAD is usually made a decade earlier in smokers than nonsmokers. The amputation rates in patients with PAD who smoke is twice higher than those that have never smoked. Smoking elevates the risk for PAD several folds and approximately 90% of persons with PAD have a history of smoking. Although the precise mechanism by which chronic smoking induces vascular disease is not entirely understood, growing evidence shows that impairment of endothelial morphology and function plays a crucial role in the pathogenesis of vascular disease. Oxidants, delivered by cigarette and deposited in pulmonary vessels through the systemic vasculature, activate superoxide producing enzymes within the vascular wall *via* oxidative stress and might be the cause of endothelial dysfunction and dysregulation of endothelial barrier. The World Health Organization (WHO) estimates that there are currently 1.1 billion tobacco smokers' worldwide ages 15 years and older. Recently, smoking-related death have been said to account for 4.9 million persons per year worldwide. Tobacco use is considered the most important preventable vascular risk factor for PAD in men and women. The association between smoking and PAD is even stronger than that between smoking and coronary disease. The connection between smoking and PAD was identified in 1911 when Erb reported that intermittent claudication was three times more common in smokers and six times more common in heavy smokers in comparison with nonsmokers.

Keywords: Peripheral arterial disease; Critical limb ischemia; Intermittent claudication; Smoking; Tobacco use; Nicotine; Atherosclerosis; Ankle brachial index test; Toe brachial index test; Vascular disease

INTRODUCTION

Atherosclerosis associated with PAD is the most common form of vascular disease seen by clinicians. However, the low recognition of the prevalence, morbidity, and mortality of PAD results in under treatment. Therefore, persons with PAD do not consistently receive long-term medical interventions that might improve their limb function and survival [1]. Peripheral artery disease interventions include lipid-lowering and hypertensive agents, smoking cessation and education, antiplatelet therapies and other risk factor reduction therapies that modify the progression of atherosclerosis and decrease the high rates of myocardial infarctions, stroke, and death. Additionally, the

prescription of exercise training, circulation medications, and selective revascularization strategies can ameliorate lower extremity ischemic symptoms and avert amputations [2].

Pathophysiology

Peripheral artery disease is narrowing of the peripheral arteries serving the legs, stomach, arms, and head ("Peripheral" in this case means away from the heart, in the outer regions of the body) [3]. Peripheral artery disease most commonly affects arteries in the legs. Acute arterial occlusion of a limb is the most common presenting symptoms of an occlusive disease to the lower leg and foot with severe foot pains at rest relieved by

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Received date: February 12, 2019; Accepted date: February 20, 2019; Published date: March 1, 2019

Citation: Fanka BW, Chaney S (2019) Tobacco Education: Reduced Risk for Peripheral Artery Disease Intern Med 9:303. doi: 10.35248/2165-8048.19.9.303.

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dependency; Pallor when foot is elevated; Absent extremity pulses; and Tissue loss (ulceration, gangrene) [4]. The peripheral arterial disease process is a generalized process that affects multiple vascular beds, including the cerebral, coronary, and peripheral arteries. It is also a systemic disorder affecting blood vessels in the cerebral vascular circulation, coronary circulation, and lower extremity arterial circulation. Atherosclerosis results from an extensive inflammatory and fibroproliferative response to insults within the vasculature leading to disruption of normal homeostasis of the endothelium. The dysfunctional endothelium leads to an increase in adhesiveness and procoagulant properties. As atherosclerotic lesions form and through the progression of the disease eventually these lesions become atherosclerotic plaques. Activated platelets can amplify the inflammatory response and lead to vasoconstriction. Furthermore, rupture of the atherosclerotic plaque occurs in advanced stages of the disease and results in the formation of thrombus and arterial occlusion. As a result atherosclerotic plaque, thrombosis, and vasoconstriction of the arteries lead to decreased blood flow in the periphery. These manifestations may result in stroke or TIA, acute coronary syndromes, intermittent claudication, or critical limb ischemia. Major atherosclerotic risk factors such as hypertension, tobacco use, high cholesterol, diabetes mellitus and family history also play a role in PAD. As nicotine is toxic to the endothelial walls of the blood vessels, tobacco use represents the major modifiable risk factor for the PAD [5]. Therefore; any form of tobacco use represents a marked increased risk of the progression of this disease.

Patients with the most severe PAD have critical limb ischemia that produces pain at rest and threatens the viability of the limb by increasing the risk for gangrene and necrosis. Peripheral artery disease is a reliable marker for cardiovascular disease. Over a 10-year period, PAD increases the risk for death due to cardiovascular disease approximately 6-fold [5]. Peripheral artery disease produces a variety of symptoms. These symptoms include intermittent claudication and ischemic resting pain, aches, tightness, tiredness, weakness, or numbness in the legs brought on by some activity and relieved by rest [6]. When peripheral arterial circulation deteriorates to a severe degree, rest pain, non-healing wounds and gangrene follow. The first step in the diagnosing PAD is a good thorough history and physical exam. The patient's symptoms are elicited by having the patient ambulate as can tolerate in order to note the duration, quality or severity of pains that are exacerbated or ameliorated by walking. A full, thorough physical examination should be performed including a full pulse examination, palpation for aneurysms, and auscultation for bruits. One often overlooked but critically important examination step is an examination of the feet. Physical exam markers of dependent rubor and elevated pallor are considered advanced markers for PAD.

METHODS

The methods of imaging for PAD include a thorough physical examination, brachial-ankle index (ABI) and Toe-brachial index (TBI) tests, ultrasound examinations, magnetic resonance angiogram (MRA) and a computed tomography angiography (CT). One of the most useful, although underutilized diagnostic

tool for detecting PAD in the office setting is the Ankle Brachial Index (ABI) test [7]. This ABI utilizes a hand-held Doppler device to help accurately measure the severity of lower extremity arterial disease. In the patients presenting with signs and symptoms of PAD, it is essential to palpate all pulses in the lower extremities when performing a physical examination. Any asymmetry in the quality of the pulses may be an indicator of PAD. The doppler instrument is used to locate the pulses in both arms and ankles, and systolic pressures are obtained using similar blood pressure cuffs. The cuffs are inflated until the doppler signal is lost and then deflated until the signal returns. The measurement is recorded for each arm and each ankle. The higher systolic arm pressure and the higher systolic ankle pressure are used to calculate the Ankle-Brachial Index. In the patient without PAD, systolic pressure in the ankle should be the same or higher than arm pressure.

BACKGROUND/SIGNIFICANCE

The prevalence of PAD is age-dependent. In the Rotterdam study (n=5,450), the prevalence of PAD based on the ankle-brachial index (ABI) test increased from 9% of subjects 55-59 years of age to 57% of patients 85-89 years of age [8]. Similarly, the prevalence of PAD (diagnosed using non-invasive tests [segmental blood pressure above-knee, below-knee, at ankle, at toe divided by brachial pressure and three measures of flow velocity in each of the femoral and posterior tibial arteries]) increased from 2.5% in subjects 40-59 years of age to 18.8% of subjects 70-79 years of age in the San Diego population study (n=624).

An article published by the New York Times in September of 2001 in title PAD Awareness, Risk, and Treatment: New Resources for Survival (PARTNERS) program, a multi-center, cross-sectional study reported a conducted PAD study at 27 sites in 25 cities and 350 primary care practices in the US from June through October 1999 [9]. The article concluded that although PAD is exceptionally prevalent among patients treated in primary care physician practices, primary care physician's knowledge of these patients is relatively low. The report likewise asserted that under-diagnosis of PAD in primary care practices is a barrier to secondary prevention strategies for the high ischemic cardiovascular risk associated with PAD in these patients.

Furthermore, to identify the prevalence of PAD in the United States (U.S.) population, as well as determining the burden of atherosclerosis in patients with PAD, the Minnesota Regional PAD Screening Program was established, and its results published in 2001. The States wide screening program goals included:

1. Determining the efficiency of screening for PAD with an Ankle Brachial Index (ABI) test of <0.85 ;
2. Determining the magnitude of atherosclerotic disease risk factors/co-morbid conditions;
3. Assessing disease-specific morbidity and health-related Quality of Life (QOL);
4. Assessing the rate of disease awareness of affected individuals with PAD and;

5. Determining the intensity of medical intervention in patients with documented PAD.

There were 347 patients screened [Mean ABI=0.96]; 92 (26.5%) with PAD with Mean ABI=0.63; 255 (73.5%) without PAD with Mean ABI=1.07, the p-value with ABI of 0.000. Out of 347 people screened, one quarter had evidence of PAD as defined by an ankle-brachial index test value of less than 0.9 [9].

OBJECTIVES

Critical limb ischemia (CLI) is the most advanced form of infrainguinal PAD and revascularization is generally considered the optimal treatment for limb salvage. Vascular diseases in peripheral vessels and PAD produce a variety of symptoms. Patients with the most severe PAD have critical limb ischemia that produces pain at rest and threatens the viability of the limb by increasing the risk for gangrene, and necrosis [10]. Peripheral artery disease is a reliable marker for cardiovascular disease. Over a ten-year period, PAD increases the risk for death due to cardiovascular disease approximately 6-fold. In the U.S., 8 million adults have PAD, a number that is likely to escalate as the population ages [11].

This clinical case narrative will aim to encourage comprehensive PAD prevention strategies especially within primary care providers. The three objectives of the overall prevention approach including exercise will be to:

Reduce of limb symptoms

- Improve exercise capacity and prevent or lessen physical disability;
- Decrease the occurrence of cardiovascular events and;
- Provide tobacco education and cessation for prevention of detrimental PAD health-related outcomes.

CASE STUDY

Ms. B, 77, presented to the vascular clinic for an acute office visit. She was last seen six months ago for PAD management of a right foot ulcer. At that office visit, the right foot ulcer had completely healed. She now presents with complaints of three days of right foot severe pain, discoloration, coolness, mottling, and gangrene from mid-foot to all toes. One week before the encounter, she reported having severe disabling ischemic resting pains on 10/10 pain scale localized to her right foot when in a supine position and that woke her up at least two to three times a night. She reported taking Hydrocodone 10/325 mg one tablet by mouth every 6-8 hours around the clock for the past three days with just slight improvement of right foot pain. At the acute visit, she reported pain had significantly progressed and was unbearable almost at a constant rate as the pain was not being improved by pain medication, dangling her foot off the bed rail and changing positions.

On physical exam, Ms. B's right foot was cold to touch with extensive mottling from the ankle to the entire foot including all her toes. There were non-palpable dorsalis and pedis pedal pulses, and the use of a Doppler scan revealed non-dopplerable

dorsalis and pedis pedal pulses as well. Also, on exam, there were dry gangrenous ulcers to the third, fourth and fifth toes. In addition, a new open skin thickness non-pressure ulcer measuring 2.8 cm × 1.9 cm was noted to the heel with bone exposure containing moderate drainage, pus, and surrounding gangrenous base.

Ms. B's ankle-brachial index (ABI) test and toe-brachial index (TBI) test both revealed non-compressible right leg arterial results likely due to increased calcinosis secondary to her longstanding history of insulin-dependent Type 1 Diabetes Mellitus and renal failure. Pulse volume recording (PVR) waveforms were severely abnormal. Right leg arterial ultrasound ordered for ABI and TBI stenosis confirmation revealed monophasic vascular flow in the common femoral artery, profunda artery and proximal superficial femoral artery with severely decreased velocities, no vascular flow was seen in the mid-distal superficial femoral artery, popliteal, anterior tibial and posterior tibial arteries. Ordered laboratory White Blood Cell (WBC) results were 18, 000 per microliter of blood indicative of possible infection.

Ms. B. has a longstanding medical history of PAD diagnosed in 2007 secondary to her risk factors of hypertension, hyperlipidemia, Insulin-dependent Type 1 diabetes mellitus and significant tobacco use of one pack per day for over fifty years. She also has a medical history of end-stage renal disease, coronary artery disease, multiple transient ischemic strokes, a cerebrovascular accident, and left neck carotid artery stenosis. Ms. B's PAD is currently being managed with anticoagulant clopidogrel 75 mg one tablet by mouth daily and aspirin 325 mg one tablet by mouth daily. She is currently on angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and statins medications. She remains on oral glycemic along with insulin for diabetes type 1 management. Her medical comorbidities of hypertension, hyperlipidemia, insulin-dependent Type 1 diabetes mellitus, end-stage renal disease, and coronary artery disease are under her primary care clinician, nephrologist and cardiologist management.

She has a past surgical medical history of several bilateral lower extremity angiograms revascularization procedures. She is status post left leg above the knee amputation in 2015 due to PAD complications. She is status post left neck carotid artery endarterectomy in May 2017 for stroke prevention. In 2007, she underwent six heart bypasses surgeries secondary to her progressive coronary artery disease. She has undergone several venograms procedures with percutaneous transluminal angioplasty (PTA) with stent placements along with revisions of the arteriovenous graft (AVG) due to thrombosis for long-term dialysis access salvage.

Patient outcome

After discussing diagnostic test results with Ms. B., she was advised that conservative medical management measures had failed, and her right leg limb loss was imminent [12-14]. And based on her diagnostic findings and multiple endovascular revascularization procedures, she was no longer a candidate for any further vascular procedures. Ms. B. was further advised that based on Guidelines on the Management of Patients with Lower

Extremity Peripheral Artery Disease from the American Heart Association and the American College of Cardiology, the only recommended medical management at this time was a right leg above the knee amputation [15,16]. After speaking with her son privately, she verbalized understanding of proposed treatment plan but declines to proceed. She states daily unrelenting severe phantom pain despite aggressive pain management therapy due to her previous left leg amputation adding she stopped receiving hemodialysis about one week ago. She states she has decided against any further life-prolonging medical interventions or measures. Ms. B. was informed that without a right leg above the knee amputation, the gangrene on her right foot would continue to progress upward into the leg and could lead to a systemic infection requiring hospitalization. She verbalized understanding but refused to continue any further aggressive medical management. At this point, Ms. B. was referred to Palliative and Hospice Care for comfort care medical care.

Role of healthcare providers

If a patient with PAD stops smoking, the risk of severe leg pain and amputation decreases significantly. Therefore, clinicians should educate and encourage tobacco cessation programs. The potential impact of earlier PAD detection, tobacco education, tobacco cessation program management and use of outpatient preventive strategies along with effective management of PAD risk factors such as hypertension, hyperlipidemia, and diabetes mellitus play a vital role to the reduction of PAD. Ciccone et al. in an article entitled feasibility and effectiveness of a disease and care management model in the primary health care system for patients with heart failure and diabetes [2] (Project Leonardo), concluded unanimously on the importance of collaboration between the patient, physician and care management nurses to enhance positive impact on patient therapeutic interventions in disease prevention and management. The earlier PAD is diagnosed, and conservative management therapies initiated the likelihood of patients to have effective revascularization outcomes, symptom relief and quality of life [17]. Tobacco education and cessation are vital in the process of PAD management as surgeries are not always needed to repair circulatory disease. Future studies should consider the possibility of including extensive tobacco education as part of middle school and high school curriculums as part of primary prevention [18,19].

CONCLUSION

A total of \$4.37 billion was spent on PAD-related treatment and 88% of that expenditure was used for PAD inpatient care. Treatment of PAD increases with age at rates of 4.5%, 7.5%, and 11.8% for individuals aged 65-74, 75-84, and >85 years, respectively. Peripheral artery disease related costs accounted for approximately 13% of all Medicare Part A and B expenditures for the PAD-treated cohort and 2.3% of total Medicare Part A and B expenditures. The U. S.'s national PAD-related costs are high due to associated inpatient hospitalization and aging population. Smoking is a potent risk factor for symptomatic PAD, with an essential and consistent dose-response relationship. Because there are persistent higher risk factors for PAD in former smokers, tobacco control programs should not

only advocate smoking cessations, they should discourage the use of any use of tobacco products in general. It is the Doctor of Nursing Practice practitioner's role to educate the public on health care disparities and assist the population transition through complex health situations for better health outcomes and quality of life. Even though there are many options for PAD therapy including different pharmacological therapies, surgical procedures, and more recently endovascular therapy, it is essential to keep in mind that prevention before the cure is the best way of PAD management.

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