

Clinical Profile of Peripheral Arterial Disease Inpatients at Dr. Soetomo General Hospital Surabaya from 2019-2021 94

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Abstract

Background: As one of the leading causes of vascular morbidity and mortality, peripheral arterial disease (PAD) remains one of the most underdiagnosed and undertreated atherosclerotic diseases. The relatively high prevalence of PAD combined with an aging population, increasing burden of chronic diseases, and poor control of risk factors will contribute to poorer clinical outcomes in the coming decades.

Objective: This study aims to identify the clinical profile of PAD inpatients at Dr. Soetomo General Hospital Surabaya in 2019 – 2021.

Material and methods: This study is a retrospective observational descriptive study using the total sampling technique to acquire data from patients' medical records and arteriography reports diagnosed as PAD, which confirmed by arteriography examination at Dr. Soetomo General Hospital Surabaya during January 2019 - July 2021.

Results: Among 74 PAD inpatients included, PAD was more prevalent in men (52.7%) than in women. The most commonly affected age group above the age of 45. Duplex ultrasonography examination reported triphasic waveform was the most commonly found waveform on the left (33.8%) and right (39.2%) lower extremities with the left common femoral artery (55.4%) and right common femoral artery (52.7%) lower as the disease location. Arteriography examination reported complete total occlusion on the left (44.6%) and right (41.9%) lower extremities with femoral artery (51.4%) as the disease location. Critical limb ischemia (70.3%) was the most found clinical presentation among the patients. Antiplatelet agents (93.2%) were the most prescribed pharmacological agent among the patients with PAD. Patients with PAD on average were hospitalized for 6.76 days.

Conclusion: This study discovered that the vast majority PAD inpatients were men over the age of 45, with the femoral artery being the most common location for PAD lesion.

Keywords: Peripheral arterial disease; atherosclerosis; clinical profile.

1. INTRODUCTION

Peripheral arterial disease (PAD) is a progressive atherosclerotic condition that involves partial or total blockage of one or more arteries in the lower limbs and is considered an indicator of generalized atherosclerosis. As a result, "PAD" has become the preferred term for partial or complete obstruction of ≥ 1 peripheral arteries (1). This condition is sometimes referred to as peripheral vascular disease, peripheral arterial occlusive disease, and lower extremity arterial disease. Atherosclerosis is a chronic lipid-driven inflammatory disease of the artery that involves both the innate and adaptive immune systems (2). The continual exposure of vascular cells to excessive amount of lipids, combined with by endothelial activation and dysfunction in the intima layer, promotes the formation of atherosclerotic plaques. When lipids containing lipoproteins accumulate in the tunica intima and activate the endothelium, atherosclerosis progresses (3). The endothelium also expresses adhesion molecules and recruits leukocytes into the subendothelial area, where they combine with monocytes to become macrophages, which migrate into the intima tunica and generate fat

streaks, eventually leading to atherosclerotic plaque formation (4). Reduced blood flow caused by plaque obstruction or endothelial dysfunction, promotes tissue hypoxia in the lower limbs, resulting in muscle ischemia and present as the disease's symptoms, one of which is pain. The ongoing inadequate perfusion of tissue, endothelial dysfunction, chronic inflammation, and high levels of oxidative all contribute to mitochondrial injury, free radical formation, muscle fiber damage, myofiber degeneration and fibrosis, and tissue damage, which can manifest as gangrene (5).

Both atherosclerosis and PAD share overlapping risk factors. Certain factors, features, or habits may increase the likelihood for developing atherosclerosis, which can lead to PAD. Hypertension, hypercholesterolemia, diabetes mellitus, smoking, obesity, and a sedentary lifestyle are all major risk factors for PAD (6, 7). The likelihood of developing PAD increases with each risk factor, from 1.5 times with one risk factor to 10 times with three or more risk factors. A family history of PAD is also linked to a 1.83-fold increased risk of PAD and a stronger relationship with PAD with a more severe occurrence (8).

The lower extremities artery system can be divided into three segments based on structural and anatomical characteristics: the aorto-iliac, femoro-popliteal, and infrapopliteal arteries (9). PAD often affects the lower extremities and can be present in any of these segments, but the femoro-popliteal is thought to be the most commonly affected (10). Despite the fact that over 90% of cases are asymptomatic, individuals who develop symptomatic cases of PAD tend to have a history of claudication, which appears as cramp-like muscle pain that occurs with exertion and subsides quickly with rest (11, 12). Besides from intermittent claudication, abnormal or absent pedal pulses, other clinical findings include paresthesia, impaired gait, ischemic and rest pain, gangrene or non-healing wounds, pallor, and vascular bruits.

The American College of Cardiology/American Heart Association Practice Guidelines (ACC/AHA) classify the clinical presentation of PAD into four categories, namely asymptomatic PAD, intermittent claudication, critical limb ischemia (CLI), and acute limb ischemia (ALI) (13). The Fountaine and Rutherford classification is another that stratifies PAD based on its clinical presentation (14). A comprehensive history and physical examination are particularly beneficial in diagnosing PAD. Several procedures, including ankle-brachial index (ABI) measurement or other vascular imaging, such as duplex ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), and arteriography to evaluate the arteries in PAD, are necessary to confirm and help classify the risk. The primary goal of PAD management is to improve the patient's quality of life by minimizing symptoms and vascular morbidity and mortality (15). Lifestyle modification, cholesterol reduction, blood pressure control, antiplatelet therapy, anticoagulant therapy, and peripheral vasodilators are all used to treat PAD and can reduce vascular mortality, symptoms, and complications.

2. MATERIAL AND METHOD

This is a retrospective observational study that uses a total sampling technique to obtain data. Between January 2019 and July 2021, data were obtained from the electronic medical records and arteriography reports of PAD inpatients at Dr. Soetomo General Hospital Surabaya. The inclusion criteria were patients diagnosed with PAD. This study used SPSS software to analyze the data statistically.

3. RESULTS

A total of 81 cases were suspected as PAD at DR. Soetomo General Hospital Surabaya between January 2019 and July 2021, but only 74 cases of PAD were confirmed in medical records and patients' arteriography reports. The characteristics of the patients are summarized in Table 1.

Among the 74 confirmed cases, 39 (52.7%) were men, and patients over the age of 45 were the most affected. Pain in the leg (95.9%) was the most commonly reported chief complaint by patients. Critical limb ischemia (CLI) was the most commonly apparent clinical presentation seen in 52 patients (70.3%). Antiplatelet agents (93.2%) were the most commonly prescribed pharmacological agents in PAD patients.

To help confirm the PAD case and analyze the affected arteries, duplex ultrasonography and arteriography were performed on patients. On duplex ultrasonography examination, triphasic waves and common femoral artery lesions were the most common clinical findings. The most common clinical findings discovered during an arteriography examination were complete total occlusion and femoral artery lesions. The clinical findings of vascular imaging are summarized in Table 2.

Vital sign results were within the normal range. The complete blood count (CBC) results were also within the normal limits, except for decreased Hb and HCT levels and increased MCHC levels. Patients with PAD spent an average of 6.76 days in the hospital. The vital signs, CBC test results, and patient length of stay are summarized in Table 3.

Table 1. Characteristics of PAD patients

Characteristics	Frequency	Percentage (%)
Sex		
Male	39	52.7
Female	35	47.3
Age		
<25	0	0
26-35	2	2.7
36-45	9	12.2
46-55	21	28.4
56-65	21	28.4
>65	21	28.4
Chief complaint		
Pain	71	95.9
Pulseless	0	0
Pallor	0	0
Paresthesia	34	45.9
Paralysis	4	5.4
Poikilothermia	12	16.2
Necrotic foot	14	18.9
Others	24	32.4
Clinical presentation		
Asymptomatic	0	0
Claudication	0	0

Acute Limb Ischemia	22	29.7
Critical Limb Ischemia	52	70.3
Pharmacological agents		
Angiotensin-converting enzyme inhibitors (ACE inhibitor)	35	47.3
Angiotensin II receptor blockers (ARB)	17	23.0
Beta blockers	31	43.0
Calcium channel blockers (CCB)	20	27.0
Diuretic	20	27.0
Antiplatelet	69	93.2
Anticoagulant	57	77.0
Statin	41	55.4
Antidiabetic	21	28.4

Table 2. Vascular imaging results

		Left		Right	
		Frequency	Percentage (%)	Frequency	Percentage (%)
Duplex Ultrasonography	Waveform				
	Monophasic	19	25.7	19	25.7
	Biphasic	24	32.4	27	36.5
	Triphasic	25	33.8	29	39.2
	No description	16	21.6	16	21.6
	Disease location				
	Common femoral artery	42	55.4	39	52.7
	Deep femoral artery	21	28.4	19	25.7
	Superficial femoral artery	32	43.2	33	44.6
	Popliteal artery	36	48.6	33	44.6
	Posterior tibial artery	34	45.9	27	36.5
	2/3 Proximal anterior tibial artery	33	44.6	31	41.9
	1/3 Distal anterior tibial artery	33	44.6	31	41.9
	Dorsalis pedis artery	30	40.5	26	35.1
	Peroneal artery	1	1.4	0	0
	No description	16	21.6	16	21.6
	Stenosis degree				
	Insignificant	24	32.4	15	20.3
	Significant	17	23.0	20	27.0
	Complete total occlusion	33	44.6	31	41.9
	No description	9	12.2	9	12.2
Arteriography					

Disease location				
Abdominal aorta	6	8.1	6	8.1
Common iliac artery	10	13.5	12	16.2
External iliac artery	8	10.8	14	18.9
Internal iliac artery	4	5.4	5	6.8
Femoral artery	38	51.4	38	51.4
Popliteal artery	25	33.8	17	23.0
Anterior tibial artery	34	45.9	34	45.9
Posterior tibial artery	18	24.3	20	27.0
Peroneal artery	3	4.1	6	8.1
Dorsalis pedis artery	8	10.8	8	10.8

Table 3. Vital signs, CBC results, and length of stay of PAD patients

	Mean $\pm$ SD	Median
Vital signs		
Temperature ($^{\circ}$ C)	36.62 $\pm$ 0.33	36.60
HR (/minutes)	81.45 $\pm$ 14.08	80.00
RR (/minutes)	19.23 $\pm$ 1.22	20.00
SBP (mmHg)	124.42 $\pm$ 17.77	120.50
DBP (mmHg)	75.53 $\pm$ 9.21	78.00
CBC result		
Hb (g/dL)	12.32 $\pm$ 2.31	12.90
HCT (%)	37.08 $\pm$ 6.24	38.20
RBC ($10^6/\mu$ L)	4.37 $\pm$ 0.90	4.34
PLT ($10^6/\mu$ L)	324.86 $\pm$ 186.72	281.50
WBC ($10^3/\mu$ L)	10.59 $\pm$ 5.52	9.29
MPV (fL)	10.01 $\pm$ 1.01	9.85
MCHC (g/dL)	33.36 $\pm$ 1.76	33.50
RDW-CV (%)	14.13 $\pm$ 2.16	13.60
RDW-SD (fL)	43.73 $\pm$ 4.74	43.25
Length of stay (LOS)	6.76 $\pm$ 6.73	3.00

4. DISCUSSION

Peripheral arterial disease (PAD) is a global vascular disorder that is estimated to impact more than 200 million people globally. PAD patients are found to have a 6.6-fold increased risk of death from coronary heart disease (CHD) than patients without PAD and a 3.1-fold greater mortality rate from all causes. Despite being endemic throughout the world, PAD remains underappreciated by both the medical establishment and the general people as a substantial source of morbidity and mortality.

In this study, the incidence of PAD was higher in men compared to women. Previous studies have reported similar results on PAD incidence between men and women (16, 17). It has long been believed that estrogen is associated with a preventative effect on the onset of atherosclerotic disease in women (18). Although the vasoprotective mechanism of estrogen has not been fully understood, it is thought to occur due to increased antioxidant activity, low LDL levels, and increased HDL levels, along with the anti-inflammatory effect of estrogen. Women have smaller arterial diameters compared to age-matched segmental diameters in men, which are presumed to cause them to have a greater rate of stenosis (19). On the contrary, men are reported to have a wider plaque area than women (20). Adverse cardiovascular events are thought to be well predicted by the area of plaque and not by the degree of stenosis, suggesting that the extent of vessels affected by plaque may be more predictive than the single site affected.

PAD prevalence and incidence are closely age-related. This study discovered that PAD was extremely common in patients over the age of 45. Previous studies have also reported that the highest incidence of PAD was found in various age groups above the age of 45 (21, 22). Because PAD is inextricably linked to the physiological aspects of aging in blood vessels, its prevalence rises as the population ages. These physiological aspects include thickening of the tunica intima and media (vascular remodeling) and gradual loss of arterial elasticity, which results in vascular stiffness (23). Furthermore, there is mounting evidence that cellular senescence promotes atherosclerosis by impairing survival due to the accumulation of nuclear and mitochondrial DNA damage, increased ROS, and a proinflammatory state (24).

Depending on the severity of the disease, PAD may appear with a variety of signs and symptoms, depending on the severity of the case. In this study, pain in the leg appeared to be the most common chief complaint reported by patients. Pain in the leg that is induced by activity and relieved by rest is known as intermittent claudication and is regarded to be the hallmark of PAD. This restricted or blocked arteries that supply the muscles of the lower extremities limit the increased blood flow during activity, resulting in a disproportion between metabolic demand and oxygen supply and being associated with the development of claudication (25). This supply and demand mismatch creates transient ischemia in the muscles that manifests as pain, cramps, or fatigue. PAD patients typically have sufficient collateral blood flow that they only have symptoms during activities that increase energy demands, such as walking (26).

PAD is a spectrum of diseases ranging from asymptomatic to chronic. Critical limb ischemia (CLI) is the most severe form of the disease. In this study, CLI was the most prevalent clinical presentation in patients with PAD. CLI is characterized as a progressive claudication that may develop into nocturnal rest discomfort and can cause tissue loss in the form of ulcers or gangrene (27, 28). The clinical presentation of CLI depends on the degree of ischemia, the presence of an infection, which can exacerbate pain even in the absence of severe ischemia, and concomitant neuropathy that can cause tissue injury or hide pain due to the ulcer process (29). Many of the CLI findings in this study may be attributed by patients who only recently reported their complaints that had been prevalent for 6 months to a year earlier. In addition to clinical findings, the diagnostic criteria for CLI are also based on the duration of the onset of complaints, namely, that CLI is characterized as pain in the lower extremities during rest for more than two weeks or afternoons that do not heal within 4–12 weeks with optimal therapy or the presence of gangrene (tissue necrosis) in the feet or toes; or chronic ischemic resting pain; nocturnal recumbent pain; or ischemic skin lesions that may include ulceration or gangrene that present for at least two weeks (30, 31);

A systematic and thorough clinical examination, comprising a vascular history and physical examination, supplemented by targeted examinations, is the best way to establish the diagnosis of PAD in all patients. Advanced imaging studies may be utilized to determine the extent and location of the disease. In this study, the triphasic waveform was shown to be very common in PAD patients using duplex ultrasonography. Although spectral waveforms in normal, healthy arteries are generally, they can also be detected in mild disease with a 1–19% decrease in artery diameter (32). Another study found that despite having a triphasic

waveform, patients could acquire artery stenosis of 1–19%, and that increasing peak diastolic velocity raises the proportion of stenosis to 20–49% (33). As for the degree of stenosis, using arteriography, we discovered that complete total occlusion was the most common clinical finding in PAD patients. PAD of the lower limb is a group of atherosclerotic disorders ranging from mild plaque accumulation to persistent complete arterial blockage. Arterial narrowing or occlusion in PAD causes a steady decline in blood supply to the limbs, affecting the disease's severity. The presence of arterial stenosis, which advances progressively to create full blockage of the artery, is the pathophysiologic mechanism by which arterial insufficiency develops.

Vascular imaging techniques, such as duplex ultrasonography and arteriography, among other vascular imaging modalities, were used to provide thorough anatomic and hemodynamic information on the afflicted arteries. According to duplex arteriography data, the common femoral artery was the most prevalent location of PAD lesions, whereas the femoral artery was the most afflicted among the patients in arteriography. This disparity could be attributed to different reporting systems as well as the sensitivity and specificity of the tests. When compared to arteriography, duplex ultrasonography has a sensitivity of 80% and a specificity of 90–100% for detecting femoral and popliteal disease, but it is less reliable for assessing the severity of stenoses in the tibial and peroneal arteries (34). The predilection for certain anatomical sites may be preferred due to variances in wall composition, artery diameter, or hemodynamic variables (35). Atherosclerotic lesions are mainly observed in atheroprone locations, which are predominantly found in the branches and curvature of major arteries (36). Low, non-uniform, and irregular artery wall shear stress disrupts the endothelial barrier, making it more permeable to lipoproteins, resulting in the accumulation and sequestration of LDLs in the intima. Furthermore, the superficial placement of the common femoral artery, deep femoral artery, proximal superficial femoral artery, and popliteal artery makes it more accessible to obtain samples for tests (37). The location of the disease has been linked to a variety of clinical outcomes associated with PAD. Even after adjusting for risk factors, comorbidities, and resting ABI, patients with distal disease had a poorer prognosis than patients with proximal disease (38). The location of the lesion also influences operative outcomes and the possibility of limb salvage in patients with CLI (39).

The mainstay of symptomatic PAD treatment is antiplatelet therapy. According to the findings of this study, antiplatelet therapy was the most commonly prescribed pharmacological agent among the patients. In patients with established atherosclerosis, antiplatelet medications constitute a therapeutic cornerstone in the secondary prevention of cardiovascular events (40). Platelets play an important role in atherogenesis because they emit platelet-derived growth factor (PDGF) and serotonin (5-hydroxytryptamine, 5HT) and stimulate the smooth muscle cells migration and proliferation, resulting in atherogenesis. PAD is also linked to platelet hyperaggregability and enhanced adhesion, as well as with increased expression of the surface protein P-selectin (41). These mechanisms, along with the platelets' prominent role in the atherothrombotic complications of PAD, are the grounds for the use of antiplatelet agents in the management of PAD. The American Heart Association/American College of Cardiology (AHA/ACC) recommends the use of antiplatelet agents in symptomatic PAD patients to lower the risk of myocardial infarction (MI), stroke, and vascular mortality in patients with symptomatic PAD (42).

The length of stay for PAD patients varies per case. A more severe PAD case may necessitate a longer hospital stay. Patients with severe PAD who have pre-existing lesions and foot gangrene are frequently admitted from the emergency room to medicine services prior to the vascular consultation (43). Furthermore, the length of stay is also determined by the intricacy of each case, logistical requirements, and collaboration with other specialties, such as podiatric or plastic surgery. A demographic group with less affordable medical care at the early stages of the disease is expected to be more likely to develop a critical case while hospitalized, resulting in a patients; length of stay being extended.

5. CONCLUSION

According to the findings of this study, PAD affected men more than women. This condition was most common in patients over the age of 45. The most prevalent chief complaint was noted to be pain. The femoral artery was the most common site of PAD lesion, with critical limb ischemia being the most common clinical presentation observed in patients. Patients were generally prescribed with antiplatelet agents and spent an average of 6.76 days in the hospital due to PAD.

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