

## Prevalence of Peripheral Arterial Disease in Patients with Acute Coronary Syndrome and the Main Risk factors

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### Funding information

Self-funded

### Conflict of interest

None declared by author

Received : January, 2023

Published: March, 2023

DOI: 10.5281/zenodo.7884920

### ABSTRACT

**Background:** Acute Coronary Syndrome (ACS ) is the most serious pathology during the clinical course of coronary heart disease (CHD). Peripheral arterial disease (PAD) is often under estimated. With the use of Ankle brachial index (ABI) diagnosis of PAD can done easily and increase the detection rate of asymptomatic patients.

**Objective:** To assess the frequency of PAD and its risk factors among group of Iraqi patients presented with acute coronary syndrome.

**Patients and Methods:** This was a cross sectional study conducted at Imam Hussein Medical City in Karbala province during the period August 2021 to December. 2022. A total of 100 patients presented with acute coronary syndrome during the study period were enrolled regardless their age or gender.

**Results:** Peripheral arterial disease was reported in 40 cases (40%) of them 60% were asymptomatic. A significant association was found between higher frequency of PAD and each of older age, male gender, family history of CAD, hypertension, dyslipidemia, diabetes mellitus, current smoking, and higher body mass index, ( $P. value < 0.05$ ). Severe PAD associated with having more than one risk factor.

**Conclusion:** Peripheral artery disease particularly asymptomatic was frequent in patients with acute coronary syndrome. PAD. Older age, male gender , family history of CAD, hypertension, dyslipidemia, diabetes mellitus, current smoking and higher body mass index were significant risk factors of PAD in ACS patients , presence of more than one risk factor, increases the risk of having more sever PAD.

**Keywords:** Acute Coronary Syndrome, Peripheral Arterial Disease, Ankle brachial index , Risk factors

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## 1. INTRODUCTION

Acute Coronary Syndrome (ACS ) is the most serious pathology during the clinical course of coronary heart disease (CHD). The danger of the situation lies in the fact that ACS, unlike chronic coronary artery disease, is characterized by a rapid (hours) and sometimes rapid (minutes) course of the disease, a high risk of adverse outcomes (sudden coronary death, myocardial infarction) and requires urgent measures to save the lives of patients . The term "acute coronary syndrome" includes such clinical conditions as unstable angina and myocardial infarction. Despite the progress made in the diagnosis and treatment of ACS, the number of patients with unstable angina and myocardial infarction is steadily increasing throughout the world. According to the latest data, CAD is the most common cause of death worldwide, particularly in the low and middle income countries, estimates have shown that about 7 million deaths occur annually due to CAD (1–3). The clinical manifestations of ACS are increasing pain behind the sternum of a pressing, squeezing or burning nature, which are paroxysmal in nature and are called unstable or progressive angina. During angina attacks, pain can also be localized in the left or right half of the chest, in the epigastric or interscapular region, radiate to the lower jaw, shoulder, wrist joints and upper limbs. A distinctive feature of unstable angina pectoris is that angina pain provoked by much less than in the chronic course of coronary artery disease, physical activity or appear at rest (spontaneously), more often at night or in the early morning hours. In such situations, patients are forced to take nitroglycerin more often than usual Unstable angina occurs, as a rule, in patients with long-term coronary artery disease, with atherosclerotic lesions of the heart vessels (coronary arteries) (4,5). The risk factors for acute coronary syndrome are the same as for other types of heart disease. Old age, high blood pressure, high blood cholesterol, smoking , Lack of physical activity, unhealthy diet, obesity or overweight, diabetes, family history of chest pain, heart disease, or stroke (6). Peripheral arterial disease (PAD) or endarteritis obliterans is an inflammatory disease that most often affects the arteries of the lower extremities, less often the upper ones, in which blood vessels narrow (atherosclerosis), normal blood flow is disturbed, leading to insufficient blood supply to the tissues of the lower extremities. PAD of the legs differs in three types depending on their localization: pelvic (iliac artery), femoral

(femoral arteries) and lower leg (leg and foot arteries) (7,8). Thrombosis of the infra-renal abdominal aorta, or aortoiliac occlusive disease known as Leriche Syndrome (LS), leads to circulatory disorders in both legs with pain in the buttocks and thighs. Peripheral arterial occlusion is quite common in population over the age of 50, but only in one third of cases the disease has severe symptoms, and it occurs four times more often in men than in women. Depending on the type and severity of symptoms, PAD is classified into four stages; I-IV (9). The main risk factors for the development of atherosclerosis and PAD include: smoking, diabetes mellitus (Diabetes mellitus), high blood pressure (arterial hypertension), metabolic disorders due to obesity. Other risk factors include gender (men suffer from atherosclerosis more often than women), age, heredity, malnutrition (for example, excessive consumption of fats, meat and insufficient vegetables and fruits), overweight (obesity), lack of movement and physical loads(9–12). In order to confirm the diagnosis in case of suspected PAD, a series of clinical examination and investigations must be followed. The course of the disease depends on many factors and, in particular, on how successfully one can cope with the main cause of vasoconstriction - atherosclerosis. To a large extent, it depends on the patient himself, on how actively and consistently he himself will deal with risk factors. This is, first of all, quitting smoking and controlling the possible disease of diabetes with the help of medications. Despite the fact that atherosclerosis cannot be completely cured, the disease process can still be slowed down or even stopped (13–15). We aimed in this study to assess the frequency of PAD in patients presenting with acute coronary syndrome and determine the association of PAD with different risk factors of coronary artery disease.

## 2. METHODOLOGY

This was a cross sectional study conducted at Imam Hussein Medical City in Karbala province during the period from August 2021 to December 2022, included (100) patients with documented diagnosis of acute coronary syndrome. All patients were evaluated clinically and appropriate investigations were performed.

Patient with chronic renal failure( define as creatinine clearance less than 30ml/min , according to Cockcroft formula ) were excluded from the study

### **Data collection:**

Data were collected using a pre-constructed data collection sheet including the demographic and clinical parameters of the patients; age, gender, family history, history of chronic diseases, status of dyslipidemia , smoking, body mass index and other demographic variables.

### **Definitions:**

#### *Acute Coronary Syndrome (ACS):*

An atherosclerotic plaque rupture, fissuring, erosion, or a combination of these, together with intracoronary thrombosis, can all result in acute myocardial ischemia, which is referred to as the acute coronary syndrome (ACS). ACS covers a variety of myocardial infarctions, including unstable angina, ST-elevated myocardial infarction, and non-ST-elevated myocardial infarction (UA). In contrast to UA, when these cardiac biomarkers are not released into the blood, STEMI and NSTEMI are identified based on elevated cardiac biomarkers such CK-MB or Troponin-I (16).

#### *Peripheral arterial disease (PAD):*

Peripheral arterial disease (PAD) is the clinical manifestation of is the clinical manifestation of atherosclerotic and thromboembolic processes which mainly affect the peripheral arteries. Aorta, its visceral branches, and the arteries of the upper and lower limbs are all can affected by PAD (17,18). In this study, we focused on the chronic occlusive arterial disease of the lower limbs. The primary clinical symptom of PAD is intermittent claudication and is defined as pain, cramping, discomfort or fatigue in the legs that brought on by ambulation or exercise and relieved by rest. It occurs due to insufficient blood supply. It obligate the patients to stop walking or exercise due to intolerable discomfort (19). However, resting

without changing positions quickly alleviates the discomfort. Critical limb ischaemia (CLI), with intense pain and discomfort even when the patient is at rest. CLI symptoms typically occur and worsen at night when the legs are horizontal and these symptoms improve when the legs are in a dependent position (20).

#### **Measurement of ABI:**

In this study we used ABI to evaluate PAD and it was measured using a standard sphygmomanometer and a Doppler examination with an 8-MHz continuous-wave probe. After at least 30 minutes of repose in a supine position, the patient's upper and lower extremities' blood pressures were measured.

The ankle-brachial index (ABI), was determined according to the scientific statement of the American Heart association (21) by dividing the higher of the two brachial systolic blood pressures by the higher systolic blood pressure of either the dorsalis pedis artery or the posterior tibial artery . Each leg's ABI was calculated separately, and analysis was based on the lower of the two results. The ABI of less than 0.9 in at least one leg indicates the presence of PAD; however, ABI between 0.9 – 0.4 indicates a mild to moderate and an ABI of less than 0.4 indicates severe PAD (22)

#### **Statistical Analysis:**

Data were entered, managed and analyzed using the statistical package for social sciences version 25 (SPSS 25), descriptive statistics of variables presented as frequencies and percentage for categorical variables and as mean and standard deviation for scale variables. Categorical variables were compared using chi-square test or Fisher's exact test when applicable. All statistical tests and association were performed at a level of significance of  $\leq 0.05$ , to be significant

### **3. RESULTS**

A total of 100 patients were recruited in this study. All patients presented with ACS. Majority, 70%, of cases aged 65 years or older, compared to 26% at the age between 55-64 years and the least frequent, 4%, aged 45-54 years, which reflects that prevalence of ACS increases with the advancing age (positive association between), (P. value  $< 0.05$  ). Among the studied group, majority were males, contributed for 70%. family history of CAD reported in 68 cases, hypertension in 71, current smoking in 72, dyslipidemia in 69, diabetes mellitus

in 75 and body mass index of 25 kg/m<sup>2</sup> and higher reported in 78 cases, (**Table 1**). Regarding PAD, it was found in 40 cases giving a prevalence of 40% among ACS cases, (**Figure 1**). In patients with ABI<0.90, 60% were asymptomatic. Prevalence of PAD has been shown to be significantly increases with the advancing age; among cases aged 45-45 years, only one case had PAD (25%) compared to 5 (19.2%) in those aged 55 – 64 years and 34 (48.6%) in those aged 65-75 years, (P. value <0.05). Furthermore, PAD was significantly associated with male gender where it was more frequent in males, 48.6% in males compared to 20% in females, (P.value<0.05). Also, higher prevalence of PAD was associated with positive family history of CAD compared to those with negative family history of CAD; 50% vs. 18.8%, respectively, (P.value<0.05). PAD was significantly more frequent in cases with hypertension, current smoker, cases with dyslipidemia , diabetic and those with BMI of 25 kg/m<sup>2</sup> or higher, in all comparisons, (P.value<0.05), (**Table 2**). The PAD cases were further sub grouped according to the number of atherosclerosis risk factors they did have, this distribution revealed that among the 40 PAD cases, 24 (60%) had only one and 16 (40%) had more than one risk factor , (**Figure 2**). From other point of view, according to ABI value, among the 40 PAD cases 12 (30%) had severe PAD and 28 (70%) had mild-moderate PAD, (**Figure 3**). Further analysis was performed using cross-tabulation for the association between severity of PAD and number of atherosclerosis risk factors reported in PAD cases, this analysis revealed that cases with more than one atherosclerosis risk factors were more likely to have severe PAD compared to those with only one risk factor, 56.3% vs. 12.5%, respectively, (P. value < 0.05), (**Table 3**).

Table 1. Baseline characteristics of ACS patients (N=100)

Variable	No.	%	
Age (year)	45 – 54	4	4.0
	55 – 64	26	26.0
	65 - 75	70	70.0
Mean age (SD)	65.9 (SD)		
Gender	Male	70	70.0
	Female	30	30.0
Family History of CAD	Yes	68	68.0
	No	32	32.0
Hypertension	Yes	71	71.0
	No	29	29.0
Smoking history	Current smoker	72	72.0
	Non smoker	28	28.0
Dyslipidemia	Yes	69	69.0
	No	31	31.0
Diabetes mellitus	Yes	75	75.0
	No	25	25.0
BMI (kg/m <sup>2</sup> )	≥ 25	78	78.0
	< 25	22	22.0

SD: standard deviation

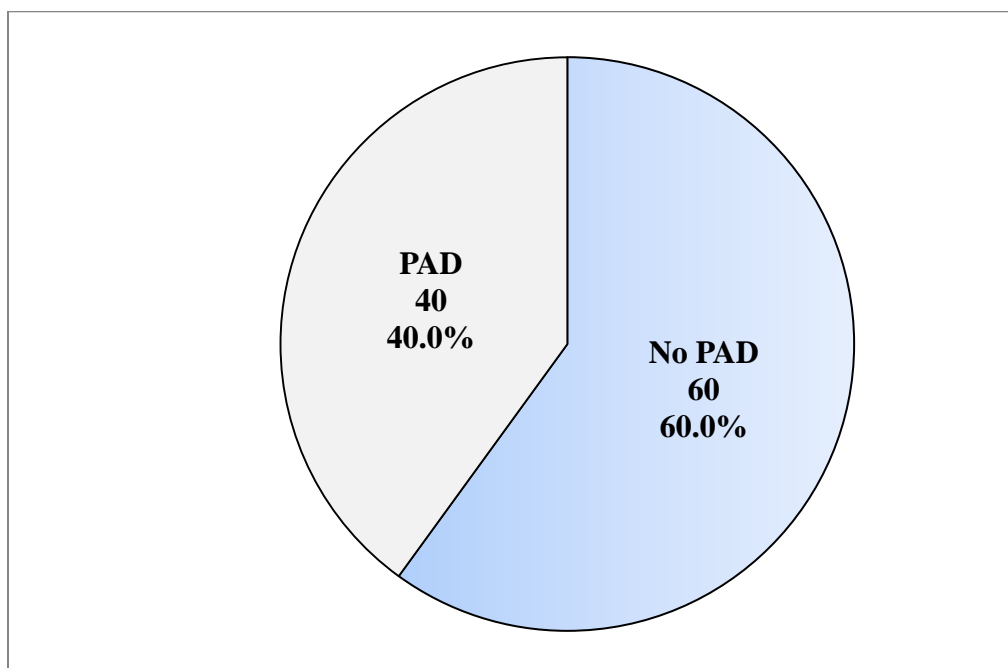


Figure 1. Prevalence of PAD among 100 ACS patients

Table 2. Cross-tabulation for possible risk factors and PAD among the studied group

Risk factor	PAD (n= 40)		No PAD (n= 60)		Total	P. value	
	No.	%	No.	%			
Age (year)	45 – 54	1	25.0	3	75.0	4	0.027
	55 – 64	5	19.2	21	80.8		
	65 - 75	34	48.6	37	51.4		
Gender	Male	34	48.6	36	51.4	70	0.007
	Female	6	20.0	24	80.0		
Family History of CAD	Yes	34	50.0	34	50.0	68	0.006
	No	6	18.8	26	81.3		
Hypertension	Yes	35	49.3	36	50.7	71	0.003
	No	5	17.2	24	82.8		
Smoking history	Current smoker	36	50.0	36	50.0	72	0.001
	Non smoker	4	14.3	24	85.7		
Dyslipidemia	Yes	34	49.3	35	50.7	69	0.005
	No	6	19.4	25	80.6		
Diabetes mellitus	Yes	36	48.0	39	52.0	75	0.005
	No	4	16.0	21	84.0		
BMI (kg/m <sup>2</sup> )	≥ 25	36	46.2	42	53.8	78	0.018
	< 25	4	18.2	18	81.8		

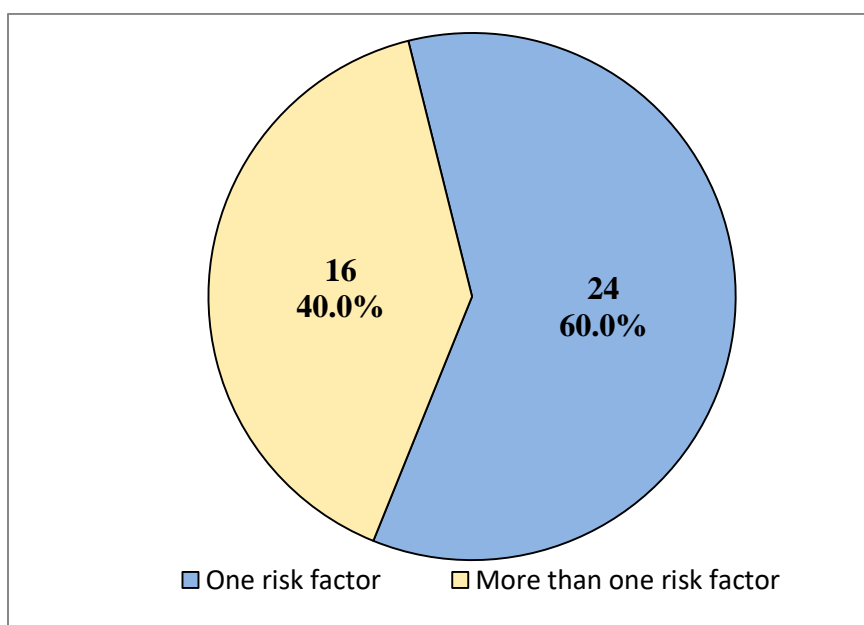


Figure 2. Distribution of number of atherosclerosis risk factors among 40 PAD cases



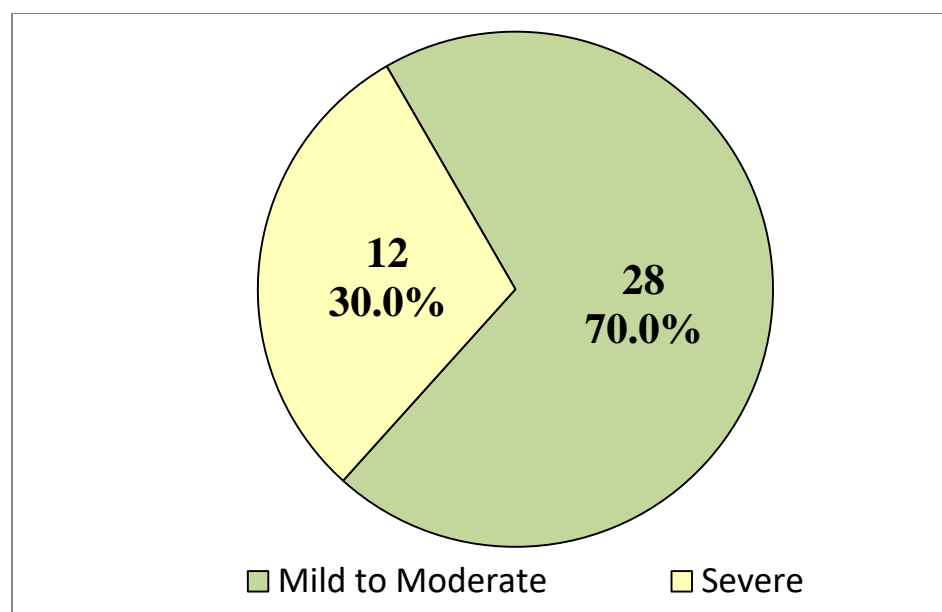


Figure 3. Severity of PAD according to ABI in PAD cases (N=40)

Table 3. Cross-tabulation for the association between severity of PAD and number of atherosclerosis risk factors reported in PAD cases

Atherosclerosis risk factor	Ankle brachial index (ABI)					
	Severe		Mild to Moderate		Total	
	No.	%	No.	%	No.	%
> One	9	56.3	7	43.7	16	40.0
One	3	12.5	21	87.5	24	60.0
Total	12	30.0	28	70.0	40	100.0

P. value = 0.005

#### 4. DISCUSSION

In our study, 40% of patients with ACS also had PAD and 60% of these patients had no symptoms. A study conducted in Saudi Arabia also found almost similar result (23), and revealed that 45% of individuals who initially report with CAD have PAD, and 61% of them were asymptomatic. However, there is a wide range in the prevalence of PAD in ACS patients

which ranges between 1% and 39% , for instance in a study included 6705 consecutive cases with ACS from 6 Arab Gulf countries, the prevalence of PAD was only 2.6% (24–26).

The correlation between ABI detected PAD and higher CAD prevalence has been demonstrated. The fact that atherosclerosis is a systemic disease supported by the idea that its presence in one artery indicates its presence in another, which reflects that atherosclerosis is a comprehensive systemic disease. This is supported the findings of our study, where 40% of patients who had ACS concurrently had PAD. Interestingly, more than half of the low ABI cases in our study were asymptomatic. This is consistent with other studies showing that intermittent claudication is the most common sign of symptomatic PAD. These findings also reported in earlier studies (27,28).

In our study, asymptomatic PAD was identified by ABI measurement, however, previous studies have demonstrated that ABI is a reliable clinical test to identify subclinical PAD (29,30). In our analysis, there were significant risk factors for atherosclerosis and PAD including age, male gender, hypertension, diabetes, dyslipidemia, family history of CVD, smoking, and obesity. ABI of 0.4 is considered to be a severe PAD, and patients with multiple atherosclerotic risk factors were shown to have a considerably greater frequency of severe PAD. Selvin et al. backed this conclusion based on findings among 2174 cases below 40 years of age and demonstrated that PAD cases had one or more risk factors (31).

In our study a higher percentage of ACS and PAD associated with older ages, which was consistent with earlier research that showed PAD and CAD progressively increase with aging (32,33). Researchers from the Framingham Heart Study grouped patients by age and estimate the ten-year risk for the occurrence of cardiovascular events, they found that the risk ranged between 3% in patients aged 30-34 years and 30% in those aged 70-74 years (34). We documented that PAD was more frequent in men. Conversely, two previous studies documented different findings, the first study found that incidence of PAD was equivalent in both genders, while the other study documented higher incidence in women (35,36).

Our study found a statistically significant relationship between PAD and each of hypertension and DM, Dyslipidemia, smoking and Obesity. However, obesity itself, increases the risk of hypertension, dyslipidemia, and insulin resistance as well as being a risk factor for cardiovascular disease, nonetheless, traditional cardiovascular risk factors have

been linked to peripheral arterial disease (PAD) and coronary artery disease (CAD) (37–42). The risk factors for atherothrombosis, specifically hypertension, diabetes mellitus, smoking, hyperlipidemia, advanced age, and obesity, make up the majority of the risk and patients who have both PAD and CAD are more likely to have these risk factors (16,26,37–43).

## **5. CONCLUSIONS**

Concomitant PAD is frequent among ACS patients. PAD is frequently asymptomatic in ACS patients. ABI has increased the detection rate of asymptomatic PAD in patients presenting with ACS. Risk factors of cardiovascular diseases are shared and commonly found in cases with PAD and CAD. The common risk factors include older age, male gender, hypertension, diabetes mellitus, dyslipidemia, family history of CAD, smoking and being overweight or obese. Atherothrombotic diseases have to be managed and approached as systemic diseases as they tend to be systemic rather than individual involvement of vascular beds. Therefore, approaches and strategies should be focused on the active screening for the early detection of PAD in ACS cases. Physicians and cardiologists should be aware about the risk factors of atherosclerosis in these patients giving attention for intensive treatment of the modifiable risk factors to decrease morbidity and mortality in ACS patients. ABI measurement is recommended in clinical practice. However, further studies are recommended for further assessment.

### **Ethical Approval:**

All ethical issues were approved by the author. Data collection and patients enrollment were in accordance with Declaration of Helsinki of World Medical Association, 2013 for the ethical principles of researches involving human. Signed informed consent was obtained from each participant and data were kept confidentially.

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**Citation:**

Sabri N.M.M Prevalence Peripheral Arterial Disease in Patients with Acute Coronary Syndrome and the Main Risk factors. *AJMS 2023; 9 (1): 29*