



Original Article

The relationship between the coexistence of coronary artery disease and peripheral arterial disease in high cardiovascular risk patients in an angiographic study; A neglected crucial link

Reza Ghasemi¹, Mahmood Hosseinzadeh Maleki², Saeideh Imani Moghaddam³,
Fatemeh Ramezani³, Hamid Hoseinikhah⁴, Mohsen Yaghubi⁵ ✉

¹ Assistant Professor, Department of Cardiology, 9 Day Hospital, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran

² Associated Professor, Department of Cardiac Surgery, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

³ Department of Critical Care, Razavi Hospital, Mashhad, Iran

⁴ Assistant Professor, Department of Cardiac Surgery, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

⁵ Department of Extra-Corporeal Circulation (ECC), Razavi Hospital, Mashhad, Iran

Corresponding Author:

Tel: +989367780472

Email: n.m.yaghubi@gmail.com

Abstract

Introduction: Peripheral arterial disease in coronary artery disease (CAD) is associated with poor cardiovascular outcomes. This issue is more highlighted in patients undergoing coronary artery bypass graft surgery after catheterization procedures.

Methods: This study was observational on participants who recourse to the heart clinics and candidates for coronary angiography, based on inclusion and exclusion criteria. In the first, coronary angiography was performed, and so, if the patients had significant involvement of coronary arteries and had at least one inclusion criteria, for assessment of peripheral arterial disease (PAD), peripheral angiography through the femoral artery was performed. The statistical analysis was done by SPSS software (Version 16) and the data were analyzed using the descriptive statistics method, variance analysis, and Fisher's Exact Test. The level of significance was considered to be (0.05).

Results: Among all patients, there was no significant difference in the demographic variables such as gender ($P=0.497$) and age ($P=0.069$). The commonest peripheral artery involved in patients was the right femoral artery. A statistically significant relationship between gender and PAD was seen ($P=0.001$). There was no significant relationship between the type of involved coronary artery and gender ($p=0.043$; Fisher's Exact Test = 10.719).

Conclusion: More than one-third of participants with CAD had peripheral arterial involvement in iliofemoral arteries in this study. This situation increased the risk of complications in vascular blind catheterization. So, Improving PAD detection is crucial for more effective cardiovascular prevention and treatment.

Keywords: Coronary Artery Disease, Peripheral Artery Disease, Coronary Angiographym

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Introduction

Owing to the increase in life expectancy and improvements in the treatment of illnesses, chronic diseases are increasing (1). Cardiovascular Diseases CVDs are the cause of concern because they are the most common chronic diseases of the 21st century and are the leading cause of disabilities and deaths worldwide (2). It is estimated that by 2020, ischemic heart disease (IHD) will be the most frequent cause of death. Until 2008, CVD was considered the first cause of mortality in Iran in people older than 35 years. Based on these data, it is evident that CVD is the most dangerous and fatal disease, with coronary artery disease CAD accounting for a large percentage of CVDs (3). In terms of pathology, the most common cause of CVD is atherosclerosis. This pathological process begins many years before clinical symptoms and evolves progressively. This process will not manifest symptoms as long as it does not involve more than 60% of the vessel diameter. Atherosclerosis also causes peripheral arterial disease PAD in the extremities, a CVD with a high prevalence, particularly in its asymptomatic form (4,5). Although PAD has attracted little attention, patients with PAD have high morbidity and mortality rates. The population prevalence of PAD, the atherosclerotic occlusive disease of arteries distal to the aortic bifurcation, ranges from 6.9% to 21.4%, depending on PAD definition, sex, and age range in Western countries. The natural history of patients with PAD is also affected by the coexistence of CAD and cerebrovascular disease (6-8).

The identification of sensitive markers for CAD diagnosis is the greatest goal of any cardiologist, and the potential of PAD as a sensitive marker of CAD and cerebrovascular disease (9). There is Also the crucial link between CAD and PAD with the patient's outcomes after cardiac surgeries, especially in coronary artery bypass graft surgeries (1). the purpose of this study was to determine the existence of PAD in patients with high cardiovascular risk factors based on angiographic findings.

Materials and Methods

The present study was a cross-sectional study that

started in March 2014 and was completed in December 2018. The study sample included all the patients who visited the heart clinics of Imam Reza and Ghaem hospitals in Mashhad, Iran. All the patients were considered candidates for coronary angiography based on electrocardiographic characteristics and the results of the exercise tolerance test, perfusion scan, and other non-invasive cardiac tests.

The patients underwent angiography at the angiography centers of Imam Reza and Ghaem hospitals. The inclusion criteria in this study were: patients with CAD showing PAD symptoms, the coexistence of CAD and PAD, patients with CAD, and the presence of tortuosity of the femoral, iliac, and aorta on angiography.

The patients included in the study underwent laboratory tests for levels of low-density lipoprotein, high-density lipoprotein, total cholesterol, triglyceride, blood urea nitrogen, and creatinine. The presence of other comorbidities such as hypertension, diabetes mellitus, dyslipidemia, and tortuosity of the femoral, iliac, and aorta was recorded.

The history of smoking was also recorded. Physical examination included evaluating peripheral pulses, poikilothermic extremities, and hair loss on the extremities, shiny and tight skin, and capillary filling. Additionally, intermittent claudication, erectile dysfunction, and sores on the feet or legs were considered positive PAD indicators.

All the participants were enrolled in the study after considering the inclusion and exclusion criteria and obtaining the patients' consent (after getting approval from the university's ethics committee). The required study sample size was estimated to be 114 based on the hypothesis of a similar study. (Mean deviation $S = 1.46$ and $d = 0.05$) (10).

First, coronary angiography was performed. If the patients displayed a significant involvement of the coronary arteries (more than 50% of the coronary artery lumen) and met at least one inclusion criterion, pigtail catheter insertion was requested before the completion of angiography. Then, the catheter was inserted into the iliac artery and placed in the aortic bifurcation through the femoral artery sheath. Afterward, 25 ml of radiopaque dye was injected

in straight view, and fluoroscopic image recording of the knee was performed. After the procedure, the patients were transferred to the recovery unit. Participants without complications were transferred to the post-angiography unit.

The exclusion criteria were: hemodynamic disturbances during angiography, existing coagulation disorders, need for cardiopulmonary resuscitation (CPR), and the absence of significant coronary artery involvement based on angiography findings. Patients who had peripheral vascular embolization and those who had had endovascular surgery and peripheral vascular bypass graft were also excluded.

A No. 16 catheter (Haryana, India) was used to access the femoral artery for cauterization.

The cutter used was the same in all the patients; the Judkins right, left, and pigtail guiding catheter series were used at 3.5, 4, 5, and 6 mm curvatures. Guidewires 0.035 and 0.038 cm in diameter were also used. The demographic variables were age and sex. The statistical analysis was performed using the Statistical Package for the Social Sciences SPSS software (Version 16). The data were analyzed using the descriptive statistics method, variance analysis, and Fisher's exact test. The significance level was considered to be (0.05).

The aim of the study was explained to the patients, and their written informed consent was obtained following the Declaration of Helsinki. Furthermore, the patients were informed that they could withdraw from the study at any time.

This study was approved by the ethics committee of Mashhad University of Medical Sciences in March 2014 (No: 910893) and complied with the Declaration of Helsinki. Informed consent was obtained from all the subjects.

Results

The number of participants in this study was 114. Of these patients, 59 (52%) were male, and 55 (48%) were female. Their mean age was 61.76 ± 8.20 years. Among the patients, no significant differences in demographic variables such as sex ($P = 0.497$) and age ($P = 0.069$) were found.

In the evaluation of the most common risk factors of CAD, diabetes mellitus was the most prevalent (56.1%), followed by smoking (44.7%), hypertension (32.5%), and dyslipidemia (18.4%).

(Table 1) shows a significant relationship between risk factors (diabetes mellitus, smoking, and dyslipidemia) and sex. In the investigation of PAD, right iliac artery involvement was observed in 5 patients, and seven patients had left iliac artery involvement.

The results showed that the right femoral artery was the most involved. Other findings of peripheral arterial involvement are shown in (Table 2).

Among the participants with PAD (stenosis of 50%), 14 were male, and nine were female. A statistically significant relationship was found between sex and PAD ($P = 0.001$). No significant relationship was found between the type of involved coronary artery and sex ($P = 0.043$; Fisher exact test, $P = 10.719$).

The findings showed that 67 patients had single-vessel disease: left main coronary artery involvement in 3 patients, left anterior descending artery involvement in 29 patients, left circumflex coronary artery involvement in 16 patients, and right coronary artery involvement in 19 patients.

Among the participants, 23 had the two-vessel disease, 17 had the three-vessel disease, and 7 had the four-vessel disease. No significant relationship was found between the number of involved coronary arteries and sex and age ($P = 0.343$; Fisher's exact test, $P = 3.409$, $p = 0.091$, and $P = 2.110$, respectively).

The investigation of PAD and CAD risk factors revealed that the incidence of PAD had no significant relationship with smoking ($P = 0.765$; Fisher's exact test, $P = 4.402$), hypertension ($P = 0.283$; Fisher's exact test, $p = 4.410$), dyslipidemia ($P = 0.174$; Fisher's exact test, $p = 8.212$), tortuosity of the aorta ($P = 0.692$; Fisher's exact test, $P = 5.099$), and clinical symptoms ($p = 0.216$; Fisher's exact test, $P = 8.212$).

No significant relationship was found between diabetes mellitus ($P = 0.034$; Fisher's exact test, $P = 11.236$) and PAD. Moreover, among the participants, no significant relationship was found between CAD and PAD ($P = 0.079$).

Table 1. Distribution of the coronary artery risk factors among patients based on gender. (*=Significance)

Risk factors/ Gender		Male	Female	Total	Statistical Test
Diabetes	Yes	21 (35.6%)	43 (78.2%)	64 (56.1%)	P<0.001*
	No	38 (64.4%)	12 (21.8%)	50 (43.9%)	
	Total	59 (100%)	55 (100%)	114 (100%)	
Hypertension	Yes	17 (28.8%)	20 (36.4%)	37 (32.5%)	P= 0.390
	No	42 (71.2%)	35 (63.6%)	77 (67.5%)	
	Total	59 (100%)	55 (100%)	114 (100%)	
Smoking	Yes	37 (62.7%)	14 (25.5%)	51 (44.7%)	P<0.001*
	No	14 (37.3%)	41 (74.5%)	63 (55.3%)	
	Total	59 (100%)	55 (100%)	114 (100%)	
Dyslipidemia	Yes	4 (6.8%)	17 (30.9%)	21 (18.4%)	P= 0.001*
	No	55 (93.2%)	38 (69.1%)	93 (81.6%)	
	Total	59 (100%)	55 (100%)	114 (100%)	
Tortuosity of the femoral, iliac and Aorta	Yes	10 (16.9%)	6 (10.9%)	16 (14.0%)	P= 0.354
	No	49 (83.1%)	49 (89.1%)	98 (86.0%)	
	Total	59 (100%)	55 (100%)	114 (100%)	
Positive clinical symptoms	Yes	3 (5.1%)	3 (5.5%)	6 (5.3%)	P= 0.999
	No	56 (94.5%)	52 (94.5%)	108 (94.7%)	
	Total	59 (100%)	55 (100%)	114 (100%)	

Table 2. Involved peripheral arteries in angiographic findings.

Involved peripheral artery	of stenosis %	(%) Number of patients
Right iliac artery	≥50%	3 (2.63%)
Right iliac artery	<50%	2 (1.75%)
Left iliac artery	≥50%	3 (2.63%)
Left iliac artery	<50%	4 (3.51%)
common iliac artery	<50%	4 (3.51%)
Right femoral artery	≥50%	6 (5.26%)
Left femoral artery	≥50%	3 (2.63%)
Left femoral artery	<50%	2 (1.75%)
Bilateral femoral artery	<50%	2 (1.75%)
Bilateral iliac& femoral arteries	≥50%	4 (3.51%)
Bilateral iliac& femoral arteries	<50%	3 (2.63%)
Iliac& right femoral arteries	≥50%	2 (1.75%)
Iliac& left femoral arteries	≥50%	2 (1.75%)
Normal findings		74 (64.91%)

Discussion

This study aimed to determine the correlation between CAD and PAD as comorbidities in patients with high risk for cardiovascular diseases based on angiography findings. The most important finding of this study was that the right femoral artery was the most involved vessel. This result has not been reported previously (4, 10-14).

Nevertheless, this finding explains why the right femoral artery is the most common artery for angiographic examinations. Our study shows that the right femoral artery was more stenotic than the other arteries.

No significant relationship was found between CAD and PAD in our study. This finding contradicts the findings of some other studies (7, 10, 13, 15). A necessary explanation for this discrepancy may be due to different population distributions in our findings rather than in other studies.

Our results showed significant correlations of cardiovascular risk factors such as smoking, dyslipidemia and diabetes with sex. This finding is similar to a study by Rafie et al. that showed a significant relationship between sex and cardiovascular risk factors (11). In other investigations, there was no significant relationship between sex and cardiovascular risk factors. (12,13,16).

The difference in observations could be the sampling of patients; the other studies had a sampling pattern such as random sampling, but in our study, samples were selected based on the study objective. In addition, the significant sex-related differences observed in this study may be related to the selection bias.

The sex-related differences among the participants with PAD were significant. Other studies 14, 16 showed the same results as our investigation. Meanwhile, the relationship between sex and CAD was not significant in this study. Other studies showed similar findings (12-14).

No significant relationship was found between the type of coronary artery involved and sex. Heravi et al. showed different results (16). In their paper, the authors mention that the type of coronary artery

involved has a statistically significant correlation with sex. By contrast, in our study, we found that the numbers of involved coronary arteries had no significant relationship with sex and age, consistent with the results of other studies (13, 16).

In our study, only diabetes mellitus significantly correlated with PAD. Vakili et al. showed a significant correlation between diabetes mellitus and hypertension (10). In another study, diabetes mellitus and hyperlipidemia had significant relationships with PAD (14).

The differences in the results of these studies may be due to the differences in race and other characteristics of the study population. A unique feature of the present study was angiography to determine the involvement and severity of PAD in the participants. Other studies used the ankle-brachial index or ultrasonography to assess patients with PAD. The advantage of the tools used in our study was the precise determination of the involvement of peripheral arteries. (12-15, 17, 18).

This study had some limitations, such as potential selection bias, and clinical nature, with a relatively high prevalence of different PAD findings in the study population. Other studies suggest that in patients with risk factors of multiple coronary diseases or diagnosed as having CVD, a peripheral injection with a radiopaque medium is needed before coronary angiography. Owing to the prevalence and effect of PAD on the prognosis of patients with CAD, the treatment of PAD is highly recommended. Also, based on this crucial link between CAD and PAD, PAD detection in catheterization procedures has an influential role in cardiac surgery plans and is even more effective in inpatient management.

Conclusion

In our study, 20.17% of the patients had significant involvement in the femoral and iliac arteries, and sex and diabetes mellitus showed significant relationships with PAD development. In addition, more than one-third of the participants with CAD had peripheral involvement of the iliofemoral arteries in significant and non-significant forms. This increased the risk of complications in vascular blind

catheterization. Thus, improving PAD detection is crucial for more effective prevention and treatment of cardiovascular events, especially in patients with the probability of cardiac surgery procedures.

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Conflicts of interest

The authors declare that they have no conflict of interest.

References

1. Fathi M, Valaei M, Ghanbari A, Ghasemi R, Yaghubi M. Comparison of Patient's Kidney Function Based on Kidney Disease Improving Global Outcomes (KDIGO) Criteria and Clinical Parameters in Isolated Coronary Artery Bypass Graft (CABG) Surgery in On-Pump and Off-pump Methods in Patients with Low Cardiac Output Syndrome (LCOS) After Surgery. *Anesth Pain Med.* 2020;10(2):e100517. doi: 10.5812/aapm.100517
2. Younessi Heravi MA, Gazerani A, Amini Z, Salimi P, Falahi Z, Yaghubi M. Pain estimation after coronary angiography based on vital signs by using artificial neural networks. *Anaesth. Pain Intensive Care.* 2021;25(1):29-34.
3. Younessi Heravi MA, Yaghubi M, Joharinia S. Effect of change in patient's bed angles on pain after coronary angiography according to vital signals. *J Res Med Sci.* 2015;20(10):937-943.
4. Alzamora MT, Forés R, Pera G, Torán P, Heras A, Sorribes M, and et al. Ankle-brachial index and the incidence of cardiovascular events in the

Mediterranean low cardiovascular risk population ARTPER cohort. *BMC Cardiovasc Disord.* 2013;13(1):1.

5. Ghasemi R, Yaghubi M. Rapid spontaneous coronary artery reperfusion following severe bradycardia during exercise tolerance test: A rare case report. *Cardiothorac Med.* 2020;8(2):639-664.
6. Gharaee R, Zohari Anboohi S, Saghi N, Malihe N, Attarroshan Y, Yaghubi M. Comparison of effects of aromatherapy with orange and bitter orange extract on sleep quality in patients with acute coronary syndrome admitted in the CCU. *J Med Plants.* 2020; 19(74): 220-228.
7. Ramos R, Quesada M, Solanas P, Subirana I, Sala J, Vila J, and et al. Prevalence of symptomatic and asymptomatic peripheral arterial disease and the value of the ankle-brachial index to stratify cardiovascular risk. *Eur J Vasc Endovasc Surg.* 2009;38(3):305-311.
8. Sigvant B, Wiberg-Hedman K, Bergqvist D, Rolandsson O, Andersson B, Persson E, and et al. A population-based study of peripheral arterial disease prevalence with a special focus on critical limb ischemia and sex differences. *J Vasc Surg.* 2007;45(6):1185-1191.
9. Ghasemi R, Dastani M, Abdolahi A, Rahimi HR. Peripheral arterial stenosis and coronary artery disease coincidence. *Reviews in Clinical Medicine.* 2014;2(1):5-8.
10. Vakili H, Sadeghi R, Doustali K, Saadat H, Namazi MH, Safi M. Evaluation of asymptomatic peripheral arterial disease by ankle-brachial index in patients with concomitant coronary arterial disease. *Int Cardiovasc Res J.* 2012;6(4):128-130.
11. Sadrzadeh Rafie A.H, Stefanick M.L, Sims S.T, Phan T, Higgins M, Gabriel A, and et al. Sex differences in the prevalence of peripheral artery disease in patients undergoing coronary catheterization. *Vasc Med.* 2010;15(6):443-450.
12. Núñez D, Morillas P, Quiles J, Cordero A, Guindo J, Soria F, and et al. Usefulness of an abnormal ankle-brachial index for detecting multivessel coronary disease in patients with acute coronary syndrome. *Rev Esp Cardiol.* 2010;63(1):54-59.
13. Sadeghi M, Heidari R, Mostanfar B, Tavassoli

A, Roghani F, Yazdekhashti S. The relation between ankle-brachial index (ABI) and coronary artery disease severity and risk factors: an angiographic study. *ARYA Atheroscler*. 2011;7(2):68-73.

14. Hussein AA, Uno K, Wolski K, Kapadia S, Schoenhagen P, Tuzcu EM, and et al. Peripheral arterial disease and progression of coronary atherosclerosis. *J Am Coll Cardiol*. 2011;57(10):1220-1225.

15. Suominen V, Rantanen T, Venermo M, Saarinen J, Salenius J. Prevalence and risk factors of PAD among patients with elevated ABI. *Eur J Vasc Endovasc Surg*. 2008;35(6):709-714.

16. Younessi Heravi MA, Mojdekanlu M, Seyed Sharifi SH, Yaghubi M. The role of cardiovascular

risk factors in involvement of coronary arteries; A predictive model in angiographic study. *JNKUMS*. 2014;6(1):199-205.(Presian)

17. Mourad JJ, Cacoub P, Collet JP, Becker F, Pinel JF, Huet D, Sevestre-Pietri MA, and et al. Screening of unrecognized peripheral arterial disease (PAD) using ankle-brachial index in high cardiovascular risk patients free from symptomatic PAD. *J Vasc Surg*. 2009;50(3):572-580.

18. Kazemi SA, Sadeghi M, Hashemi SM, Heidari R, Gharipour M, Golabchi A, and et al. Evaluating the Relation between Metabolic Syndrome and its Components with Low Ankle to Brachial Index in an Iranian Population. *Journal of Isfahan Medical School*. 2011;28(122): 1724-1732. (Presian)