Original Article

Prevalence of lower extremities peripheral arterial disease among Egyptian ischemic patients attending cardiac rehabilitation unit

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ABSTRACT

Background: Atherosclerosis is progressive and diffuse pathological disorders which can simultaneously affect multiple vascular beds. Diagnosing Lower extremities peripheral arterial disease (PAD) in patients with Coronary artery disease (CAD) admitted to cardiac rehabilitation program can help to tailor exercise regimen to fit these patients, in addition, early treatment and/or intervention may help to control progression of the disease.
Aim: The study is to search for the prevalence of undiagnosed PAD using ankle brachial index (ABI) in Egyptian patients with documented CAD undergoing cardiac rehabilitation program.
Patients and Methods: The study included 200 patients with documented CAD scheduled for cardiac rehabilitation in Cardiology department, Ain Shams University, with exclusion of patients with known (diagnosed) PAD. All patients underwent ABI using Doppler ultrasonography. The patients were divided into two groups; Study group with positive ABI (≤ 0.9) and Control group with negative ABI (> 0.9).
Results: We found that the prevalence of undiagnosed PAD in those patients was 14.5% (29 patients). The incidence of PAD is increased in patients above 60 years (p = 0.001) and in presence of hypertension/uncontrolled systolic blood pressure (p = 0.002), Dyslipidemia (p = 0.005), or family history of ischemic heart disease (p = 0.035). PAD is associated also with impaired left ventricular systolic function and presence of segmental wall motion abnormalities at rest. Impaired eGFR increased the risk of development of PAD (p = 0.016). PAD was associated more with patients presented by multivessel lesions by coronary angiography and in presence of ischemic ECG changes.
Conclusion: This study shows that significant PAD is present in almost 15% of ischemic Egyptian patients. We recommend ABI to be done routinely in patients with significant CAD for exclusion or diagnosis of PAD to help in treatment and improving quality of life in addition to modification of cardiac rehabilitation program in presence of PAD according to its severity.

1. Introduction

Atherosclerosis is a progressive and diffuse pathological disorder which can simultaneously affect multiple vascular beds. Postmortem studies confirmed that have the highest prevalence of atherosclerosis is found in the coronary arteries compared to other arterial beds.[1–3]

Lower extremities Peripheral arterial disease (PAD) is usually manifesting in concordance with systemic atherosclerotic process including coronary artery disease (CAD).[1,2] Diagnosing PAD in patients with CAD can help to change the exercise regimen prescribed to these patients in cardiac rehabilitation program to fit both pathologies, in addition to early treatment and/or intervention if required.[4–10]

ABI is the ratio of the systolic blood pressure (SBP) measured at the ankle to that measured at the brachial artery.[11] This index is not only used for the noninvasive diagnosis of PAD[12,13], but it also has a prognostic value for cardiovascular events and functional impairment, even in the absence of symptoms of PAD.[14–21]

For diagnosis of significant lower extremity PAD (more than 50% stenosis), ABI was found to have a sensitivity of more than 90% and a specificity of more than 95% in several studies, when compared to angiography.[22–27]

To the best of our knowledge, there are no published data assessing the prevalence of PAD in cardiac ischemic patients in Egypt.

Table 1
Shows main characteristics of the study population, comparing group I and group II.

Variables		PAD Status				Chi-square	P-value
		Study (n=29)		Control (n=171)			
		No.	%	No.	%		
DM	Yes	16	55.2%	77	45.0%	1.025	0.311
	No	13	44.8%	94	55.0%		
HTN	Yes	26	89.7%	66	38.6%	26.023	0.000**
	No	3	10.3%	105	61.4%		
DLP	Yes	24	82.8%	94	55.0%	7.915	0.005**
	No	5	17.2%	77	45.0%		
Smoking	Yes	20	69.0%	100	58.5%	1.136	0.287
	No	9	31.0%	71	41.5%		
Peripheral Pulsations	Present	29	100.0%	171	100.0%		
Ischemic Changes	Yes	1	3.4%	0	0.0%	5.926	0.015*
	No	28	96.6%	171	100.0%		
Intermittent claudications	Yes	12	41.4%	34	19.9%	6.470	0.011*
	No	17	58.6%	137	80.1%		
ECG Changes	Yes	27	93.1%	118	69.0%	7.222	0.007**
	No	2	6.9%	53	31.0%		
SWMA	No	0	0.0%	43	25.1%	9.290	0.002**
	Yes	29	100.0%	128	74.9%		
LV EF	Normal	10	34.5%	97	56.7%	4.931	0.026*
	Abnormal	19	65.5%	74	43.3%		
CAD presentation	STEMI	25	86.2%	87	50.9%	20.312	0.000**
	Non-STEMI	4	13.8%	10	5.8%		
	UA	0	0.0%	74	43.3%		
Coronary Angiography	MVD	6	20.7%	24	14.0%	1.960	0.743
	LAD	16	55.2%	107	62.6%		
	RCA	7	24.1%	35	20.5%		
	LCX	0	0.0%	4	2.3%		
	PDA	0	0.0%	1	0.6%		
Cholesterol	Abnormal	15	51.7%	36	21.1%	12.278	0.000**
	Normal	14	48.3%	135	78.9%		
TG	Abnormal	3	10.3%	12	7.0%	0.396	0.529
	Normal	26	89.7%	159	93.0%		
eGFR	Abnormal	14	48.3%	45	26.3%	5.749	0.016*
	Normal	15	51.7%	126	73.7%		
LDL	Abnormal	8	27.6%	48	28.1%	0.003	0.957
	Normal	21	72.4%	123	71.9%		
HDL	Abnormal	15	51.7%	87	50.9%	0.007	0.933
	Normal	14	48.3%	84	49.1%		

PAD: peripheral arterial disease, DM: diabetes mellitus, HTN: hypertension, DLP: dyslipidemia, SWMA: segmental wall motion abnormalities (by echocardiography), LV EF: left ventricular ejection fraction (by echocardiography), CAD: coronary artery disease, STEMI: ST segment elevation myocardial infarction, NSTEMI: non-ST segment elevation myocardial infarction, UA: unstable angina, MVD: multivessel disease, LAD: left anterior descending artery, RCA: Right coronary artery, Lcx: Left circumflex artery, PDA: posterior descending artery, TG: Triglycerides, eGFR: estimated glomerular filtration rate, LDL: Low density lipoprotein, HDL: High density lipoprotein

The aim of this study is to investigate for prevalence of undiagnosed lower extremities PAD using ABI among Egyptian patients with documented CAD undergoing cardiac rehabilitation program.

2. Subjects and methods

This study included (200) patients presented to (Ain Shams University -Aldemerdash- Hospital), cardiac rehabilitation clinic from January 2015 to November 2015, who had documented CAD and underwent percutaneous coronary intervention (PCI). Patients with previously diagnosed PAD and those refusing to sign the consent were excluded.

In addition to history, clinical examination, laboratory tests and echocardiography, the Ankle brachial index was measured using a portable vascular Doppler scanning (Nicolet vascular Elite, VIASYS healthcare, USA) and aneroid sphygmomanometer with appropriate cuff inflators for brachial circumference as previously described in literature[11,23,28]

ABI was considered as positive if it is ≤0.9.[28]

2.1. Statistical analysis

Categorical variables will be expressed as number (%) and continuous variables will be expressed as mean ± SD. The independent sample t-test and ANOVA will be used to compare the mean values of different groups. For all tests, p value <0.05 will be considered statistically significant. All the analyses will be performed with commercially available software (SPSS version 20.0; SPSS, Inc., Chicago, IL, USA).
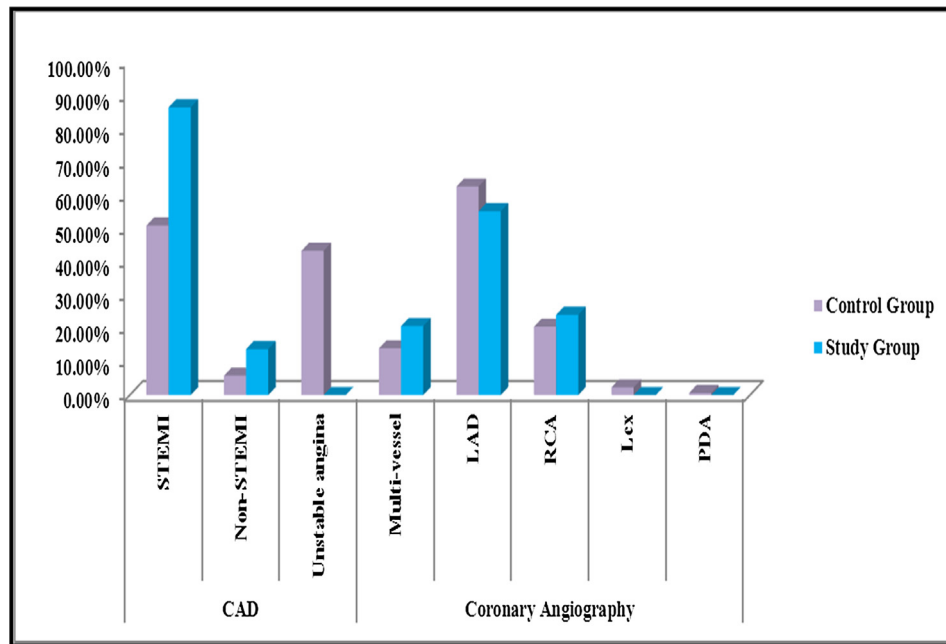
Fig. 1. Differences between study and control groups regarding presentation and details of coronary angiography. STEMI: ST segment elevation myocardial infarction, LAD: left anterior descending artery, RCA: right coronary artery, Lcx: left circumflex artery, PDA: posterior descending artery.

3. Results

This study assessed 200 patients who have a documented CAD and admitted to cardiac rehabilitation program, for detection of undiagnosed PAD using ABI. In this study, we divided the patients into two groups according to the results of ABI measurements as follows: Group I with ABI ≤ 0.9 (29 patients) and group II (control group) with ABI > 0.9 (171 patients).

The age of our studied patients ranged from 37 to 80 years with mean age of 54.73 ± 9.163 and most of our study population were males (162 patients). Our data showed that gender did not have statistically significant correlation with presence of PAD. On the contrary, prevalence of PAD was highest in those above age of 60 years and lowest below 40 years old. Table 1 shows characteristics of the study population.

Among the conventional risk factors for atherosclerotic vascular disease, only the presence of hypertension and dyslipidemia, were found to carry statistically significant difference between both groups.

In addition, there was statistically significant correlation between PAD and presence of ischemic ECG changes, Low left ventricular ejection fraction and the presence of wall motion abnormalities in echocardiography.

Moreover, there was statistically significant correlation between the presentation of ST segment elevation myocardial infarction (STEMI) and incidence of PAD. The incidence of PAD was also increased among patients with Left Anterior Descending artery (LAD) lesions and multivessel disease but did not reach statistical significance. Fig. 1 summarizes the relation between presence of PAD and the coronary vessels affected.

4. Discussion

Our study assessed 200 patients with documented CAD who underwent PCI, and joined cardiac rehabilitation program. ABI was used for detection of undiagnosed PAD, being an inexpensive, simple, and reproducible test that can be easily performed in the office or at the bedside.

In our study, the prevalence of undiagnosed PAD in patients with CAD was 14.5%. These results were concordant with Dieter et al.[29], who assessed a total of 100 patients (66 men and 34 women) and found a 19% prevalence of undiagnosed PAD. However other studies found a prevalence as high as 26.6%.[30] The difference between results may be due to the variation in number of studied patients and, different studied populations as well as prevalence of risk factors in studied patients.

Our study demonstrated increased incidence of PAD in patients over 60 years, that was previously shown in Egyptian patients where the lowest ABI values were present in patients above the age of 70 years in study group (ABI ≤ 0.9) with mean ABI of 0.708 (p < 0.001).[31] Similar data were obtained in other studies.[30]

Regarding the conventional risk factors of atherosclerosis, our study results demonstrated increased prevalence of PAD in presence of history of hypertension (89.7%) or dyslipidemia (82.2%). These results were concordant with previous studies.[29,32]

Smoking and diabetes mellitus are well known risk factors for PAD as well as CAD. Data derived from several observational studies indicate a twofold to fivefold increased risk of PAD in smokers.[33–40] Similarly, the risk of development of PAD increases threefold to fourfold in patients with DM.[34,37,38,41,42] However, our study did not show significant correlation between smoking or DM and diagnosis of PAD. This could be explained by the observation that the prevalence of each of the two risk factors was high in both groups; Our patients are already atherosclerotic with documented CAD. Analysis of our data showed that almost half of subjects in each group were diabetic and more than two thirds were smokers in each group.

In the current study, intermittent claudication was present in 41.4% (12 patients) of patients with positive ABI and in only 19.9% (34 patients) of those with negative ABI (P = 0.011), while ischemic changes in lower limbs was found in only one patient of the study who belongs to the study group. This could justify the importance of screening for PAD by adequate history taking, clinical examination and ABI.

In our study, the highest prevalence of PAD was present in patients with LAD lesions, followed by RCA lesions then multivessel disease. In addition, STEMI presentation was more associated

with PAD than other presentations of ACS. These results were in concordance with Cavalcanti et al.[43], who studied the association between ABI and coronary lesions assessed by coronary angiography, this study included 163 patients with a clinical diagnosis of stable angina. They found that LAD lesions were present in 57.6% of patients and RCA lesions occurred in 47.2% of patients and LCX lesions in 38% of patients. On multivariate Poisson regression, an ABI < 0.9 was only an independent predictor of LAD stenosis (P < 0.001). High prevalence of PAD among patients with multivessel CAD was also found in previous studies.[44]

Echocardiographic findings have been found to be a clue for PAD in our study; PAD was present in 18.4% of patients with SWMA and not present at all in patients without SWMA. Tsao and colleagues[45] studied the relation between presence of left ventricular SWMA (by MRI) and prevalence of PAD using ABI. Among 1726 patients, they found that lower ABI was associated with the presence of SWMA; (38% of patients with SWMA and in only 8% of patients without SWMA (P < 0.001)]. This high prevalence compared to the present study may be attributed to the smaller number of studied patients, different patient inclusion criteria and different methods of assessment of SWMA.

In our study, lower ABI was also associated with decreased eGFR (P = 0.016). The mean eGFR value was 73.48 in study group and 81.99 in control group (p = 0.032). Such finding is concordant with Qing and Hongbo,[46] who found that among 612 geriatric patients 24% had positive ABI, and ABI values were significantly lower in patients with decreased eGFR compared to those with normal eGFR (p = 0.000). The Chinese Ankle Brachial Index Cohort found that the prevalence of PAD in patients with and without CKD was 41.9% and 22.3%, respectively (p < 0.001) and the combined CKD and PAD patients had the highest risk for all-cause and CVD mortality.[47]

In conclusion, ABI can be used routinely in patients with significant CAD, being simple, inexpensive, non invasive and available method for exclusion or diagnosis of PAD if present as early diagnosis will help in treatment and improving quality of life in addition to modification of cardiac rehabilitation program in presence of PAD according to its severity.

5. Limitations

- The study included only 200 patients who have documented CAD and Patients with documented PAD were excluded from the study.
- Data about peripheral angiography (gold standard for diagnosis of PAD) in patients with + ve ABI was not followed in the study.

Conflict of interest

None.

References

1. Vink A, Schoneveld AH, Poppen M, de Kleijin DP, Borst C, Pasterkamp G. Marphometric and immunohistochemical characterization of the intimal layer throughout the arterial system of elderly humans. *J Anat.* 2002;200:97–103.
2. Weber G, Bianciardi G, Bussani R, et al.. Atherosclerosis and aging. A morphometric study on arterial lesions of elderly and very elderly necropsy subjects. *Arch Pathol Lab Med.* 1988;112:1066–1070.
3. Grundy SM, Cleeman JI, Merz CN, et al.. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel lll guidelines. *Circulation.* 2004;110:227–239.
4. Stewart KJ, Hiatt WR, Regensteiner JG, Hirsch AT. Exercise training for claudication. *N Engl J Med.* 2002;347:1941–1951.
5. Nehler MR, Hiatt WR. Exercise therapy for claudication. *Ann Vasc Surg.* 1999;13:109–114.
6. Girolami B, Bernardi E, Prins MH, et al.. Treatment of intermittent claudication with physical training, smoking cessation, pentoxifylline, or nafronyl: a meta-analysis. *Arch Intern Med.* 1999;159:337–345.
7. Gardner AW, Poehlman ET. Exercise rehabilitation programs for the treatment of claudication pain. A meta-analysis. *JAMA.* 1995;274(12):975–980.
8. Gibellini R, Fanello M, Bardile AF, Salerno M, Aloi T. Exercise training in intermittent claudication. *Int Angiol.* 2000;19:8–13.
9. Gardner AW, Katzel LI, Sorkin JD, Goldberg AP. Effects of long-term exercise rehabilitation on claudication distances in patients with peripheral arterial disease: a randomized controlled trial. *J Cardiopulm Rehabil.* 2002;22:192–198.
10. Hussein AA, Uno K, Wolski K, et al.. Peripheral arterial disease and progression of coronary atherosclerosis. *J Am Coll Cardiol.* 2011;57:1220–1225.
11. Aboyans V, Criqui MH, Abraham P, et al.. American Heart Association Council on Peripheral Vascular Disease; Council on Epidemiology and Prevention; Council on Clinical Cardiology; Council on Cardiovascular Nursing; Council on Cardiovascular Radiology and Intervention, and Council on Cardiovascular Surgery and Anesthesia. Measurement and interpretation of the ankle-brachial index: a scientific statement from the American Heart Association. *Circulation.* 2012;126:2890–2909.
12. Carter SA. Indirect systolic pressures and pulse waves in arterial occlusive diseases of the lower extremities. *Circulation.* 1968;37:624–637.
13. Yao ST, Hobbs JT, Irvine WT. Ankle systolic pressure measurements in arterial disease affecting the lower extremities. *Br J Surg.* 1969;56:676–679.
14. Criqui MH, Langer RD, Fronek A, et al.. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med.* 1992;326:381–386.
15. McDermott MM, Guralnik JM, Tian L, et al.. Associations of borderline and low normal ankle-brachial index values with functional decline at 5-year follow-up: the WALCS (Walking and Leg Circulation Study). *J Am Coll Cardiol.* 2009;53:1056–1062.
16. Fowkes FG, Murray GD, Butcher I, et al.. Ankle brachial index combined with Framingham risk score to predict cardiovascular events and mortality: a meta-analysis. *JAMA.* 2008;300:197–208.
17. Zheng L, Li J, Hu D, et al.. Association of low ankle-brachial index with mortality in patients with ischemic heart disease. *J Atheroscler Thromb.* 2010;17:759–767.
18. Kojima I, Ninomiya T, Hata J, et al.. A low ankle brachial index is associated with an increased risk of cardiovascular disease: the Hisayama study. *J Atheroscler Thromb.* 2014;21:966–973. Epub 2014 Apr 14.
19. Hajibandeh S, Hajibandeh S, Shah S, Child E, Antoniou GA, Torella F. Prognostic significance of ankle brachial pressure index: A systematic review and meta-analysis. *Vascular.* 2017 Apr;25(2):208–224.
20. Qu B, Liu Q, Li J. Systematic review of association between low ankle-brachial index and all-cause cardiovascular, or non-cardiovascular mortality. *Cell Biochem Biophys.* 2015 Nov;73(2):571–575. https://doi.org/10.1007/s12013-015-0582-z.
21. Bonaca MP, Bhatt DL, Storey RF, Steg PG, Cohen M, et al.. Ticagrelor for prevention of ischemic events after myocardial infarction in patients with peripheral artery disease. *J Am Coll Cardiol.* 2016;67:2719–2728.
22. Hirsch AT, Criqui MH, Treat-Jacobson D, et al.. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA.* 2001;286:1317–1324.
23. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, et al.. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation.* 2006;113:e463–e654.
24. McDermott MM, Liu K, Criqui MH, et al.. Ankle-brachial index and subclinical cardiac and carotid disease. The multi-ethnic study of atherosclerosis. *Am J Epidemiol.* 2005;162:33–41.
25. Diehm C, Schuster A, Allenberg JR, et al.. High prevalence of peripheral arterial disease and co-morbidity in 6880 primary care patients: cross-sectional study. *Atherosclerosis.* 2004;172:95–105.
26. Vogt MT, Mckenna M, Anderson SJ, Wolfson SK, Kuller LH. The relationship between ankle-arm index and mortality in older men and women. *J Am Geriatr Soc.* 1993;41:523–530.
27. Dormundy JA, Rutherford RB. Management of peripheral arterial disease (PAD). TASC Working Group. Trans Atlantic Inter Society Consensus (TASC). *J Vasc Surg.* 2000;31:201–296.
28. Grenon SM, Gagnon J, Hsiang Y. Video in clinical medicine. Ankle-brachial index for assessment of peripheral arterial disease. *N Engl J Med.* 2009;361:e40.
29. Dieter RS, Tomasson J, Gudjonsson T, Brown RL, et al.. Lower extremity peripheral arterial disease in hospitalized patients with coronary artery disease. *Vasc Med.* 2003;8:233–236.
30. Kownator S, Cambou JP, Cacoub P, et al. Prevalence of unknown peripheral arterial disease in patients with coronary artery disease. 2009;102:625–31.
31. Amer MS, Tawfik HM, Abd Elmotteleb AM, Maamoun MM. Relationship between ankle brachial index and ejection fraction in elderly Egyptians with ischemic heart disease. *Geriatr Gerontol Int.* 2015;15(4):405–409.
32. Sedaghi M, Heidar R, Mostanfar B, et al.. 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.
33. Gofin R, Kark JD, Friedlander Y, et al.. Peripheral vascular disease in a middle-aged population sample. The Jerusalem Lipid Research Clinic Prevalence Study. *Isr J Med Sci.* 1987;23:157–167.

34. Newman AB, Siscovick DS, Manolio TA, et al.. Ankle-arm index as a marker of atherosclerosis in the Cardiovascular Health Study. Cardiovascular Heart Study (CHS) Collaborative Research Group. *Circulation.* 1993;88:837–845.
35. Bowlin SJ, Medalie JH, Flocke SA, et al.. Epidemiology of intermittent claudication in middle-aged men. *Am J Epidemiol.* 1994;140:418–430.
36. Bainton D, Sweetnam P, Baker I, et al.. Peripheral vascular disease: Consequence for survival and association with risk factors in the Speedwell prospective heart disease study. *Br Heart J.* 1994;72:128–132.
37. Murabito JM, D'Agostino RB, Silbershatz H, et al.. Intermittent claudication. A risk profile from The Framingham Heart Study. *Circulation.* 1997;96:44–49.
38. Fowkes FG, Housley E, Riemersma RA, et al.. Smoking, lipids, glucose intolerance, and blood pressure as risk factors for peripheral atherosclerosis compared with ischemic heart disease in the Edinburgh Artery Study. *Am J Epidemiol.* 1992;135:331–340.
39. Criqui MH, Browner D, Fronek A, et al.. Peripheral arterial disease in large vessels is epidemiologically distinct from small vessel disease. An analysis of risk factors. *Am J Epidemiol.* 1989;129:1110–1119.
40. Lassila R, Peltonen S, Lepantalo M, et al.. Severity of peripheral atherosclerosis is associated with fibrinogen and degradation of cross-linked fibrin. *Arterioscler Thromb.* 1993;3:1738–1742.
41. Kannel WB, McGee DL. Update on some epidemiologic features of intermittent claudication: The Framingham Study. *J Am Geriatr Soc.* 1985;33:13–18.
42. Hiatt WR, Hoag S, Hamman RF. Effect to diagnostic criteria on the prevalence of peripheral arterial disease. The San Luis Valley Diabetes Study. *Circulation.* 1995;91:1472–1479.
43. Cavalcanti D, Correiaa A, Jose N, et al.. Association between ankle-brachial index and coronary lesions assessed by coronary angiography. *Cardiol Res.* 2015;6(1):216–220.
44. Nunez D, Morillas P, Quiles J, Cordero A, et al.. Usefulness of an abnormal ankle-brachial index for detecting multivessel coronary disease in patients with acute coronary syndrome. *Rev Esp Cardiol.* 2010;63:54–59.
45. Tsao CW, Gona P, Salton C, Murabito JM, et al.. Relationship between central and peripheral atherosclerosis and left ventricular dysfunction in a community population. *Vasc Med.* 2011;16(4):253–259.
46. Qing W, Hongbo Z. Association between estimated glomerular filtration rate and ankle brachial index. *Heart.* 2011;97:A231.
47. Luo Y, Li X, Li J, Wang X, Xu Y, Qiao Y, et al.. Peripheral arterial disease, chronic kidney disease, and mortality: the Chinese Ankle Brachial Index Cohort Study. *Vasc Med.* 2010 Apr;15(2):107–112.