Role of Doppler Ultrasound and Peripheral Angiography (as a Diagnostic Modality of Atherosclerosis) in Combination with Conventional Atherosclerosis Risk Factors in Coronary Artery Disease Prediction

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Abstract: Introduction: Atherosclerosis is a generalized disease; the presence of the disease at one site increases the frequency of symptomatic and asymptomatic disease at another. The conventional risk factors of smoking, hypertension, hyperlipidemia, insulin resistance and diabetes, physical activity, and obesity are correlated to systemic vascular disorders. Preclinical markers of atherosclerosis enable identification of individuals in whom the atherosclerotic process is already present. Consequently, in recent years, research on atherosclerosis has been mainly focused towards identifying markers of early preclinical atherosclerosis. The most frequently studied are circulating markers and markers of early arterial wall alteration such as arterial wall thickening. **Purpose:** was to identify the value of Doppler ultrasound and peripheral angiography (as a diagnostic modality of atherosclerosis) in combination with conventional atherosclerosis risk factors in coronary artery disease prediction. **Material and methods:** The study included one hundred patients with suspected or proven CAD; non invasive parameters such as, arterial duplex, carotid intima-media thickness, ankle-brachial index were done. Invasive investigations such as peripheral angiography (PA) and coronary angiography were done**. Result:** The study included one hundred patients, the mean age was 57.40 ± 6.32 years (ranged from 35-70 years), seventy five patients were males (75%). Forty seven patients (47%) were diabetic, seventy seven patients (77%) were hypertensive, sixty two patients (62%) were smoker, seventy one patients (71%) were dyslipedemic, forty six patients (46%) had an elevated serum cholesterol, forty four patients (44%) had an elevated serum triglycerides, forty three patients (43%) had an elevated serum LDL, thirty five patients (35%) had positive family history. **Conclusion:** nonconventional markers for atherosclerosis such as CIMT and/or ankle-brachial index (ABI) may be useful in providing a predictive value for CAD.
Combination of more than one measurement (specially the nonconventional markers) were more effective than the use of a single measurement for predicting cardiovascular events.
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Key Words: Carotid intima-media thickness, coronary artery disease, ankle-brachial index, peripheral arterial disease.

1- Introduction

Coronary artery disease (CAD) as the major cause of death in developing countries is a matter of interest in health care programs.

Preclinical markers of atherosclerosis enable identification of individuals in whom the atherosclerotic process is already present. Consequently, in recent years, research on atherosclerosis has been mainly focused towards identifying markers of early preclinical atherosclerosis. The most frequently studied are circulating markers and markers of early arterial wall alteration such as arterial wall thickening *(1).*

Earlier studies have shown an association between peripheral arterial disease (PAD) and a high risk of cardiovascular events and death in patients with or without known coronary artery disease, independent of the presence of other cardiovascular risk factors(2).

The ankle-brachial index (ABI), a simple, non-invasive measurement, shows high sensitivity and specificity in the diagnosis of peripheral arterial disease when its value is <0.9. It is also a powerful indicator of atherosclerotic disease in other vascular areas and of increased cardiovascular morbidity and mortality *(3).*

The ABI is defined, as the ratio of the systolic blood pressure in the ankle divided by the systolic blood pressure at the arm. *(4).*

The diagnostic criteria for peripheral arterial disease (PAD) based on the ABI are interpreted as follows: Normal if 0.91–1.30, Mild PAD if 0.70–0.90, Moderate PAD if 0.40–0.69, Severe PAD if less than 0.40, poorly compressible if more than 1.30. An ABI value more than 1.3 suggests poorly compressible arteries at the ankle level due to the presence of medial arterial calcification. This renders the diagnosis of PAD by ABI alone less reliable *(4).*

ABI to be inversely correlated to the extent and the severity of coronary disease, and to be one of the main variables for predicting the extent of disease, along with advanced age, diabetes mellitus, male sex, plasma high density lipoprotein cholesterol (HDL-C), the intima-medial thickness of the common femoral artery and the waist/hip ratio *(5).*

Carotid intima-media thickness (CIMT) is another established marker of subclinical atherosclerosis and is a noninvasive marker of atherosclerotic plaque at an early stage *(6).*

Imaging of the entire common carotid artery (CCA), the carotid bifurcation, the ICA as distal as possible, and the external carotid artery is the first step in carotid sonographic examination. It is the best method for measuring IMT and showing atherosclerotic plaques. Mean IMT is calculated in the CCA between 2 interfaces: blood-intima and media-adventitia. Intima-media thickness measurement can be performed either manually or by computer software *(7).*

A thickness of 1.1 mm or greater is actually a more accepted abnormal value *(8).*

The goal of noninvasive arterial duplex test and peripheral angiography in PAD in our study is to distinguish normal from diseased vessels, diseased vessel means, nonsignificant arterial disease , significant disease and occlusion , significant disease means more than 50% arterial diameter reduction.

Therefore, the expanded uses of nonconventional markers such as CIMT and/or ABI may be useful in providing a predictive value *(9).*

The combination of the two measures was more effective than the use of a single measurement for predicting cardiovascular events *(10).*

Purpose: was to identify the value of Doppler ultrasound and peripheral angiography (as a diagnostic modality of atherosclerosis) in combination with conventional atherosclerosis risk factors in coronary artery disease prediction.

2. Material and methods:

The study included one hundred patients with suspected or proven CAD; non-invasive parameters such as, arterial duplex, CIMT, ABI were done. Invasive investigations such as peripheral angiography and coronary angiography were done

Inclusion criteria;

The study included patients with suspected or proven CAD.

Exclusion criteria

Patients who refuse to participate in the study, Patients with contraindications for coronary angiography, Patients with a history of coronary bypass graft, percutaneous transluminal coronary angiography, cardiomyopathy, severe valvular heart disease, sinus node dysfunction, atrial fibrillation, conduction disturbance.

Each patient will be subjected to; Full history taking including determination of risk factors i.e. diabetes mellitus, smoking, hypertension, dyslipidemia, obesity, family history (FH) of CAD, Routine clinical examination, Lipid profile including serum cholesterol, LDL, HDL and serum triglycerides, Peripheral arterial duplex, Detection of ankle-brachial index **(**via Summit Doppler device- Vista AVS-Model-L500VA device), Detection of carotid intima media thickness(Via GE logic 9 and machine GE S6 machine- superficial probe 10 MH), peripheral angiography, Coronary angiography (Retrograde angiography using the Judkin's technique).

3.Results

Study population;

The study included one hundred patients selected randomly with suspected or proven CAD by Framingham risk scoring who were referred to Bab Al-She'ryia University Hospital between May 2012 to November 2013, the mean age was 57.40 ± 6.32 years (ranged from 35-70 years), seventy five patients were males (75%).

Risk factors;

Forty seven patients (47%) were diabetic, seventy seven patients (77%) were hypertensive, sixty two patients (62%) were smoker, seventy one patients (71%) were dyslipedemic, forty six patients (46%) had an elevated serum cholesterol, forty four patients (44%) had an elevated serum triglycerides, forty three patients (43%) had an elevated serum LDL, thirty five patients (35%) had positive family history.

Table (1): showing the significance of each conventional and nonconventional risk factors in relation to the number of diseased coronary vessels

Risk factors		No of vessels					chi-square	
		0	1	2	3	Total	X^2	P.value
Male	N	6	32	7	30	75	5.412	0.144
	%	54.55	78.05	58.33	83.33	75		
Female	N	5	9	5	6	25		
	%	45.45	21.95	41.67	16.67	25.00		
DM	N	5	13	8	21	47	7.712	0.052
	%	45.45	31.71	66.67	58.33	47.00		
HTN	N	8	36	7	26	77	5.718	0.126
	%	72.73	87.80	58.33	72.22	77.00		
SMOKER	N	5	28	5	24	62	4.304	0.230
	%	45.45	68.29	41.67	66.67	62.00		
Dyslipidemia	N	4	23	12	32	71	24.667	0.000
	%	36.36	56.10	100.00	88.89	71.00		
S cholesterol	N	2	15	8	21	46	9.529	0.023
	%	18.18	36.59	66.67	58.33	46.00		
S TG	N	2	12	6	24	44	14.718	0.002
	%	18.18	29.27	50.00	66.67	44.00		
S LDL	N	0	14	8	21	43	19.841	0.000
	%	0.00	34.15	66.67	58.33	43.00		
FH	N	0	5	4	26	35	41.267	0.000
	%	0.00	12.20	33.33	72.22	35.00		
ABI	N	0	4	7	33	44	74.019	0.000
	%	0.00	9.76	58.33	91.67	44.00		
Duplex	N	2	32	11	36	81	36.774	0.000
	%	18.18	78.05	91.67	100.00	81.00		
PA	N	2	31	11	36	80	37.211	0.000
	%	18.18	75.61	91.67	100.00	80.00		
CIMT	N	0	19	9	36	64	60.569	0.000
	%	0.00	46.34	75.00	100.00	64.00		

Table (2): showing significance of number of conventional and nonconventional risk factors in relation to the number of diseased coronary vessels

No of risk factor		No of vessels				
		0	1	2	3	Total
1	N	0	2	0	0	2
	%	0.00	4.88	0.00	0.00	2.00
2	N	6	2	0	0	8
	%	54.55	4.88	0.00	0.00	8.00
3	N	3	3	0	0	6
	%	27.27	7.32	0.00	0.00	6.00
4	N	1	12	0	0	13
	%	9.09	29.27	0.00	0.00	13.00
5	N	1	2	2	1	6
	%	9.09	4.88	16.67	2.78	6.00
6	N	0	3	2	0	5
	%	0.00	7.32	16.67	0.00	5.00
7	N	0	5	1	4	10
	%	0.00	12.20	8.33	11.11	10.00
8	N	0	8	1	4	13
	%	0.00	19.51	8.33	11.11	13.00
9	N	0	0	1	9	10
	%	0.00	0.00	8.33	25.00	10.00
10	N	0	2	5	9	16
	%	0.00	4.88	41.67	25.00	16.00
11	N	0	2	0	8	10
	%	0.00	4.88	0.00	22.22	10.00
12	N	0	0	0	1	1
	%	0.00	0.00	0.00	2.78	1.00
Total	N	11	41	12	36	100
	%	100.00	100.00	100.00	100.00	100.00
Spearman's rho	r	0.719				
	P-value	<0.001*				

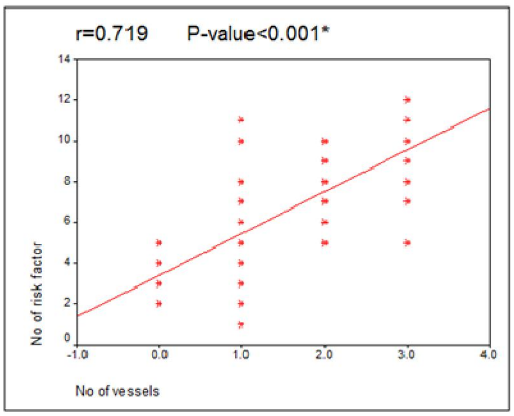
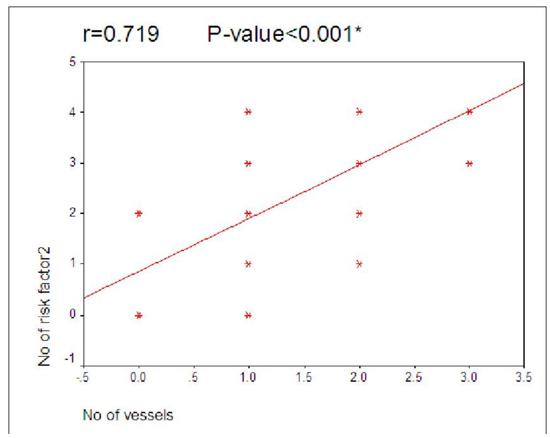


Table (3): Analysis of significance of number of non-conventional risk factors in relation to the number of diseased coronary vessels.

No of non-conventional risk factor 2		No of vessels				
		0	1	2	3	Total
0	N	9	6	0	0	15
	%	81.82	14.63	0.00	0.00	15.00
1	N	0	4	1	0	5
	%	0.00	9.76	8.33	0.00	5.00
2	N	2	15	3	0	20
	%	18.18	36.59	25.00	0.00	20.00
3	N	0	12	1	3	16
	%	0.00	29.27	8.33	8.33	16.00
4	N	0	4	7	33	44
	%	0.00	9.76	58.33	91.67	44.00
Total	N	11	41	12	36	100
	%	100.00	100.00	100.00	100.00	100.00
Spearman's rho	r	0.809				
	P-value	<0.001*				



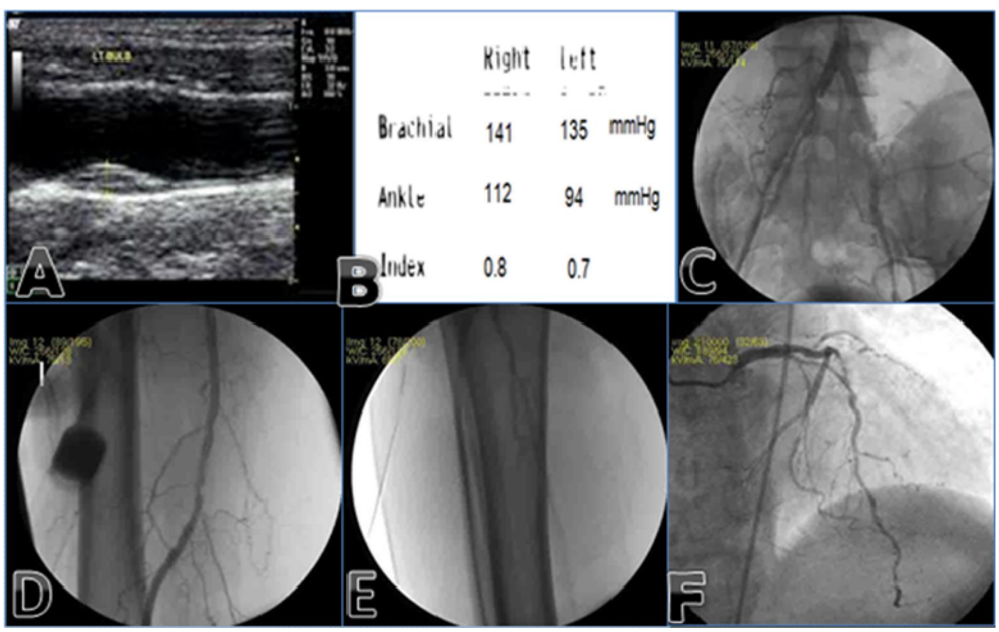


Fig. (1)

a): Increased CIMT, b): Abnormal ABI,

c): Lesions at right and left external iliac arteries

d): Right SUP femoral artery, e): Left SUP femoral artery,

f): LAD and LCX lesions, g): RCA lesion

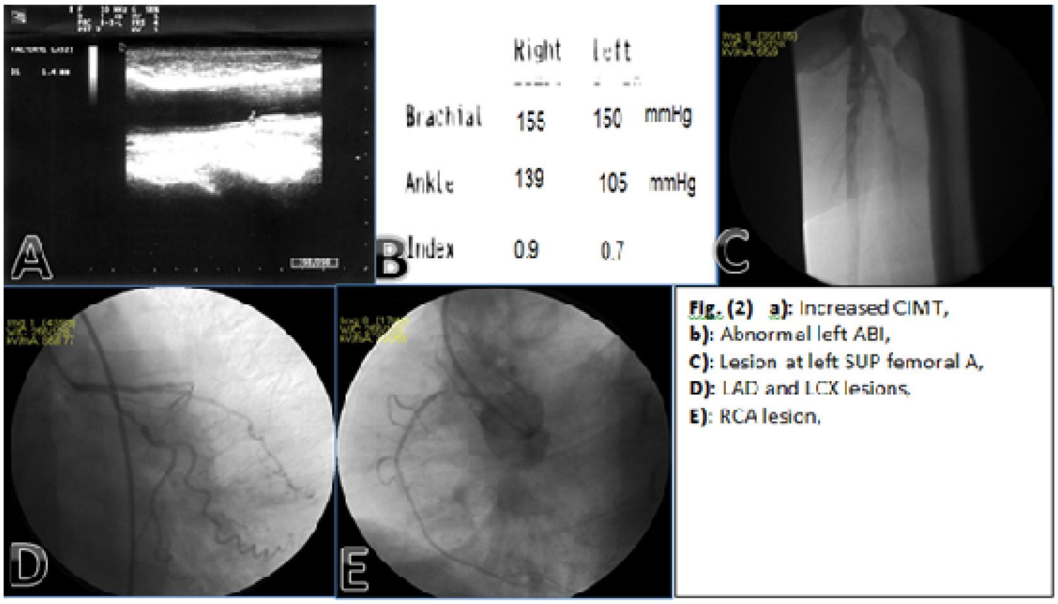


Fig. (2) a): Increased CIMT,
b): Abnormal left ABI,
C): Lesion at left SUP femoral A,
D): LAD and LCX lesions,
E): RCA lesion,

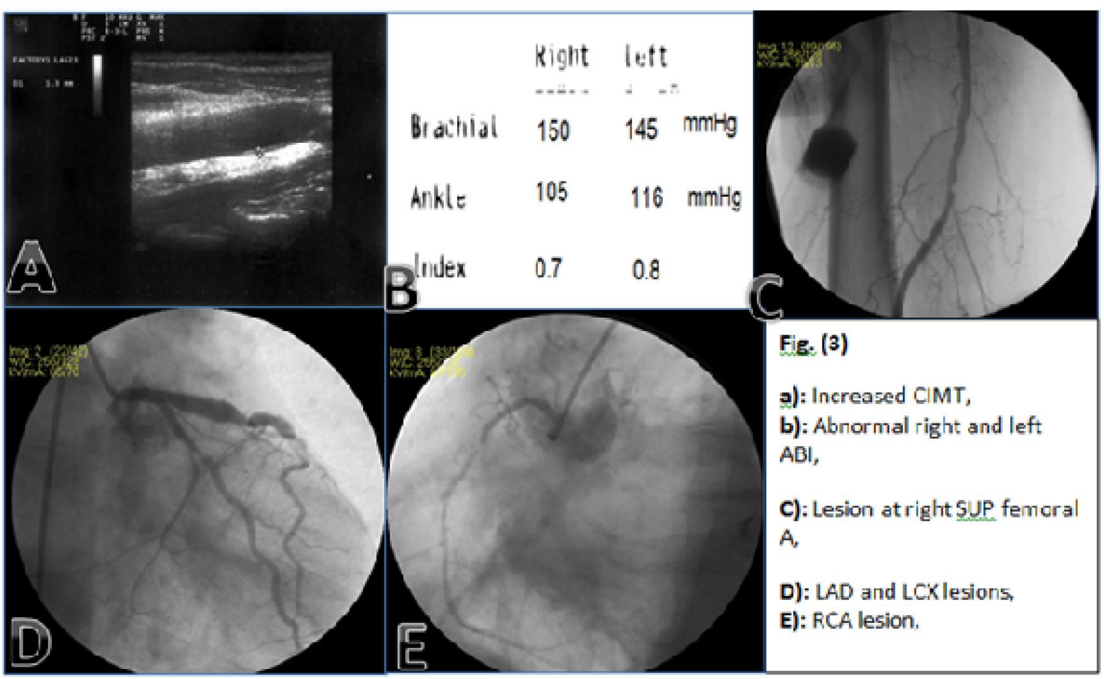


Fig. (3)

a): Increased CIMT,
b): Abnormal right and left ABI,

C): Lesion at right SUP femoral A,

D): LAD and LCX lesions,
E): RCA lesion.

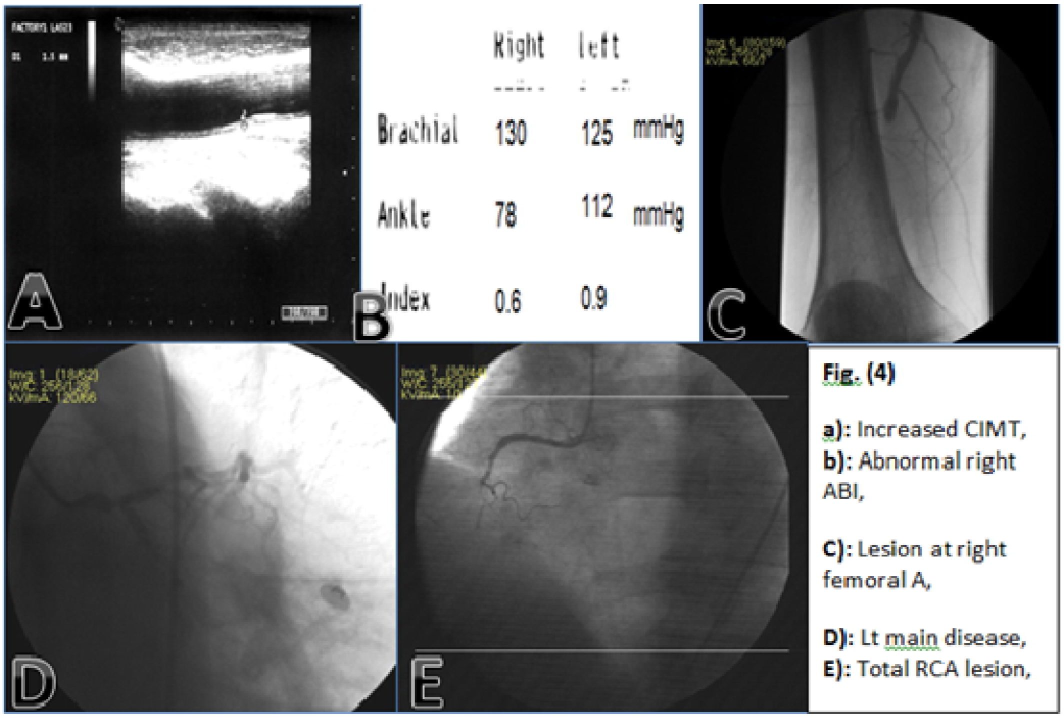


Fig. (4)
a): Increased CIMT,
b): Abnormal right ABI,
C): Lesion at right femoral A,
D): Lt main disease,
E): Total RCA lesion,

4.Discussion

Atherosclerosis is the most frequent underlying cause of ischemic heart disease (IHD) and cerebrovascular disease; thus, it is the leading cause of death in western societies.

Multisite artery disease is defined as the simultaneous presence of clinically relevant atherosclerotic lesions in at least two major vascular territories.

Given the common etiology of peripheral atherosclerosis occurring at different vascular sites, the presence of disease at one site increases the frequency of symptomatic and asymptomatic disease at another. The degree of concordance observed between sites is, however, dependent on the methods of diagnosis and on the selected population. From a clinical perspective, such findings indicate the need for a heightened awareness of the possibility of atherosclerotic disease occurring at sites other than the presenting one. This is especially so in the elderly in whom the degree of overlap of CAD, cerebrovascular disease, and PAD is particularly high *(11)*.

Interest in the non-invasive assessment of cardiovascular function has increased, particularly around the relationship between the stiffness of large arteries and blood pressure *(12)*.

The detection of PAD is of special interest since atherosclerosis is considered a generalized disease, and diagnosis of PAD frequently indicates atherosclerosis in other vessel beds *(13)*.

Definite PAD was associated with significantly higher carotid IMT. Among women, borderline ABI was associated with greater subclinical atherosclerosis in the internal carotid artery than was normal ABI. Among men, low ABI values were associated with greater subclinical atherosclerosis in the internal carotid, common carotid, and coronary arteries *(14)*.

Many studies have shown that the ABI has a high specificity and good negative predictive power with respect to coronary artery disease in patients suspected of having ischemic heart disease or more severe coronary involvement *(15)*.

The present results show that the patients with a pathological ABI had more extensive coronary disease, with a greater prevalence of multivessel disease *(16)*.

ABI less than 0.9 and ultrasonographic presence of plaque in the carotid and femoral arteries strongly and independently predict cardiovascular and total mortality during long-term follow-up. The relationship between ABI and future cardiovascular events was clearly linear *(17)***.**

Agnelli *et al.* showed that an ABI of <0.9 increased the risk of non-fatal myocardial infarction and all cause death, especially among those with the lowest indices. Similarly, the present results show that the patients with a pathological ABI had more extensive coronary disease, with a greater prevalence of multivessel disease *(16)*.

Chang *et al.* showed the usefulness of ABI for predicting complex and diffuse coronary lesions, reporting a greater proportion of lesions at the ostial level and in proximal segments in patients with an ABI of <0.9 than in those with an ABI of ≥0.9 *(15).*

In general medical practice, the prevalence of ABI <0.90 is 25–30 percent among patients with old age or with a history of diabetes or smoking. ABI <0.90 is associated with a two- to threefold increased risk of cardiovascular morbidity and mortality *(18).*

Measurement of carotid intima-media thickness (CIMT) with B-mode ultrasound is a noninvasive, sensitive, and reproducible technique for identifying and quantifying atherosclerotic burden and CAD risk. It is a well-validated research tool that has been translated increasingly into clinical practice *(19).*

CIMT values add additional information beyond traditional risk factors for classifying patients in regard to the likelihood of presence of significant angiographic coronary artery disease *(20).*

The data from more than 37,000 individuals concluded that increments of 0.1 mm in c-IMT translated to an increased risk of 10% to 15% for having a myocardial infarction and an increased risk of 13% to 18% for having a stroke. Accordingly, the clinical application of c-IMT represents a powerful, noninvasive surrogate marker of atherosclerosis, providing a meaningful end point measurement for clinical trials. The application of c-IMT has become an accepted, reliable surrogate marker for determination of atherosclerosis; c-IMT measurements represent the preferred technique for noninvasively assessing atherosclerosis in most clinical trial studies *(6).*

Conclusion

- Atherosclerosis is a generalized disease; the presence of the disease at one site increases the frequency of symptomatic and asymptomatic disease at another. Diagnosis of PAD frequently indicates atherosclerosis in other vessel beds.
- ABI has a high specificity and good negative predictive power with respect to coronary artery disease in patients suspected of having ischemic heart disease or more severe coronary involvement.
- The present results show that the patients with a pathological ABI had more extensive coronary disease, with a greater prevalence of multivessel disease so The ankle-brachial index can be used as an alarming for cardiovascular events..
- CIMT values add additional information beyond traditional risk factors for classifying patients in regard to the likelihood of presence of significant angiographic coronary artery disease.

According to our results, the expanded uses of markers of atherosclerosis are useful in providing a predictive value. The combination of more than one measurement were more effective than the use of a single measurement for predicting cardiovascular events specially if the measured risk factors are nonconventional risk factors (such as CIMT , ABI, and peripheral LL duplex) as explained above in table (3) r= 0.809, where in table(2) r=0.719**.**

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