The correlation between femoral intima-media thickness (F.IMT) and the severity of coronary artery damage in patients with coronary artery disease

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Abstracts

A pre-clinical sign of atherosclerisis is hypertrophy of arterial wall. Femoral intima-media thickness is non-invasive marker of arterial wall alteration, which can easily be assessed by high resolusion B mode ultrasound. **Aims:** To investigate the correlation between femoral intima-media thickness and the severity of coronary artery diseases. **Methods:** 111 consecutive patients with coronary artery diseases were enrolled. Femoral intima-media thickness was assessed by B mode ultrasound with 7.5 - 10 MHz probe about 10 - 15 mm before bifurcation to profond and superfacial femoral arteries. The femoral intima-media thickness < 1.0 mm is named as "normal", ≥ 1.0 mm is "thick" and ≥ 1.5 mm is defined as "atherosclerosic femoral plaque". The severity of coronary artery diseases was calculated by Gensini Score. **Results:** Mean femoral intima-media thickness was 1.57 ± 1.23 mm, 55% patients with abnormal femoral intima-media thickness (male 57.0% và female 50.0%), 36.9% of patients with coronary artery diseases had atherosclerosic femoral plaque. There was a good correlation between femoral intima-media thickness and severity of coronary artery diseases by Gensini score and its risk factors (age, plasma glucose, smoking, hypertension…). **Conclusion:** Patients with coronary artery diseases are likely to have concomittant peripheral artery disease with high frequency of femoral artery wall changes. Femoral intima-media thickness could be a helpful diagnostic marker and therapeutic points.

Keywords: *atherosclerisis, Femoral intima-media thickness, coronary artery diseases, femoral intima-media thickness (F.IMT).*

1. INTRODUCTION

Atherosclerosis has been discovered in Egypt since the 50s BC. The pathogenesis of atherosclerosis is not entirely clear. Peripheral vascular disease is an important complication of atherosclerosis. The risk factors for atherosclerosis such as smoking, diabetes, dyslipidemia, hypertension and elevated homocysteine… are also considered major risk factors for lower limb artery disease [1], [2], [11]. Lower extremity atherosclerosis, which early sign in the preclinical stage as thickening of the intima-media layer, can be detected early and accurately by Doppler ultrasound. The femoral intima-media thickness (F.IMT) is considered to be an overall cardiovascular risk factor, was strongly correlation with coronary artery damage and cardiovascular events [16], [17], [18].

From the clinical practice, the lower limb artery disease is often not properly focused, leading to a missed diagnosis, which can lead to dangerous complications for the patients because treatment is too late. Therefore, we implement this study for two purposes:

1. To assess the Femoral intima-medina thickness by Doppler ultrasound in patients with coronary artery diseases.

2. To evaluate the relationship between lower extremity artery lesions with several cardiovascular risk factors and severity of lesions to coronary artery diseases.

2. MATERIALS AND METHODS

A cross-sectional study was conducted on 111 patients with coronary artery disease in Hue Central Hospital from March 2013 to June 2014. All participants were provided with written informed consent and agreed to join our study; and the protocol was approved by the Ethical Review Committee of Hue University of Medicine and Pharmacy, Vietnam

Assessment of severity of coronary artery disease

All patients were diagnosed with coronary artery disease based on coronary angiography

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with significant lesion which was > 50% diameter of stenosis and assess its severity according to the Gensini score [3].

Bilateral Femoral Arteries Findings by Ultrasonography

Patients were guided to lay on the supine position with flexible lower extremities. According to the standardized protocol for ultrasound in Vietnam, experienced ultrasound practitioners investigated femoral arteries from the common femoral arteries to the bifurcation of the femoral artery into the superficial artery and the profunda femoral artery. Colored Doppler and continuous Doppler modes were employed to investigate the morphology and functions of arteries. The IMT was measured from the boundary of the vascular intima and lumen to the boundary of tunica media and tunica adventitia at end-diastole B-mode. IMT measurements were performed at both left and right femoral artery alternatively and the highest IMT was reported as an IMT variable for each patient, which classified into 3 categories: (i) normal IMT (less than 1mm); (ii) thick IMT (1 ≤ IMT < 1.5mm); (iii) atherosclerosis (IMT ≥ 1.5mm) based on the classification for carotid artery [9], [10], [11].

3. RESULTS

3.1. General characteristics of the study population

Table 1. General characteristics of study subjects

General features	Male (n=79)		Female (n=32)		Total		P
	n	%	n	%	n	%	
n	79	71.2	32	28.8	111	100	< 0.05
Mean age	64.48 ± 11.10		68.84 ± 9.65		65.74 ± 10.84		> 0.05
Hypertension	44	55.7	21	65.6	67	58.6	
History of coronary artery disease	32	40.51	16	50	48	43.2	
Smoking	57	72.2	0	0.0	57	51.4	
Diabetes	20	25.32	8	28.6	28	25.2	
Hypertotalcholesterolemia	29	36.7	18	56.3	47	42.3	
Hypertriglyceridemia	35	44.9	15	46.9	50	45.5	p > 0.05
Hyper-LDLCholesterolemia	23	29.1	9	28.1	32	28.8	
Hypo-HDLCholesterolemia	12	15.2	4	12.5	16	14.4	

Study subjects include 79 male patients (71.2%) and 32 female patients (28.8%). The mean age was 65.74 ± 10.84 years. There were a 58.6% patients with hypertension (55.7% male and 65.6% female). The proportion of patients who smoke was 51.4%, of which 72.2% was male and there was no female patients smoke. There were 25.2% patients with type 2 diabetes (25.32% male and 28.6% female).

3.2. Coronary artery lesions on DSA:

Table 2. Rate of lesions to the main branches of coronary arteries

Gender	Left Main (1)		Right Coronary Artery (2)		Left Anterior Descending Artery (3)		Left Circumflex Artery (4)		P
	n	%	n	%	n	%	n	%	
Male (1)	1	1.3	56	71.8	64	82.1	43	55.1	P 3,4 < 0.05
Female (2)	2	6.3	27	79.4	27	79.4	15	44.1	P 2,4; 3,4 < 0.05
Total	3	2.7	83	74.1	91	81.3	58	51.8	P2,4; 3,4 < 0.001
p (1),(2)	> 0.05								

LAD lesion is the highest at 81.3%, followed by RCA with 74.1% and LCX with 51.8%. Only 2.7% had a slight stenosis of the left main coronary artery.

Table 3. Rate of the number of lesion to the main branches of coronary arteries

	1-vessel (1)		**2-vessel** (2)		**3-vessel** (3)		**P**
	n	**%**	**n**	**%**	**n**	**%**	
Male (1)	23	29.1	27	34.2	29	36.7	p>0.05
Female (2)	7	21.9	13	40.6	10	31.3	
Total	30	27.03	40	36.04	39	35.13	
P (1) (2)	p>0.05		p>0.05		p>0.05		

The rate of 1-vessel of coronary artery was 27.03%, (male and female were 29.1% and 21.9%, respectively), 2-vessel accounted for 36.04% (male and female were 34.2% and 40.6%, respectively). There was 35.13% of patients (36.7% male and 31.3% female) have 3-vessel coronaries. Thus, the proportion of patients who have multiple vessel diseases were 72.97% (the rate of lesion to 2,3 and 4 main vessel coronaries were 36.04%, 35.13% and 1.80%, respectively).

Table 4. The severity of coronary artery lesions by the Gensini score

Diagnosis	**Male** (1)		**Female** (2)		**Total** (3)		**P** (1),(2)
	n	**Gensini**	**n**	**Gensini**	n	**Gensini**	
Stable angina	29	14.41 ± 16.10	13	8.92 ± 6.76	42	12.71 ± 14.04	< 0.01
Unstable angina	27	24.82 ± 24.66	16	20.25 ± 17.09	43	23.12 ± 22.04	
NSTEMI	7	34.67 ± 11.50	2	30.00 ± 22.63	9	33.50 ± 13.13	
STEMI	16	37.37 ± 22.88	1	10.00 ± 0.00	17	36.71 ± 23.21	
Total	79	24.48 ± 22.2	32	15.94 ± 14.82	111	22.00 ± 20.70	

The severity of coronary artery lesions calculated on the Gensini score of study subjects was 22.00 ± 20.70 points, of which 24.48 ± 22.2 points for male and 15.94 ± 14.82 points for female.

3.3. Lesions of the lower limb arteries on B-mode and Doppler ultrasound

Table 5. Average femoral intima-media thickness by gender

	Male (1)	**Female (2)**	**Total**	**P** (1),(2)
	M ± SD (mm)	M ± SD (mm)	M ± SD (mm)	
Right side (1)	1.47 ± 1.06	1.54 ± 1.18	1.49 ± 1.09	> 0.05
Left side (2)	1.40 ± 1.01	1.40 ± 1.04	1.40 ± 1.02	
F.IMT (3)	1.56 ± 1.10	1.59 ± 1.19	1.57 ± 1.23	
P (1) (2)	> 0.05	> 0.05	> 0.05	

The mean thickness in male was 1.56 ± 1.10 (mm), in female it was 1.59 ± 1, 19 (mm) and for both gender was 1.57 ± 1.23 (mm).

Table 6. Mean F.IMT by number of damaged coronary vessels

Age group	**1-vessel (1)**		**2- vessel (2)**		**3-vessel (3)**		**P** (1), (2), (3)
	n	X ± SD (mm)	**n**	X ± SD (mm)	n	X ± SD (mm)	
Male	23	1.10 ± 0.86	27	1.43 ± 0.90	29	2.07 ± 1.28	< 0.05
Female	7	1.43 ± 1.15	13	1.22 ± 1.01	10	2.06 ± 1.26	
Total	30	1.18 ± 0.93	40	1.36 ± 0.92	39	2.06 ± 1.25	

The mean of the femoral intima-media thickness in patients with 1-vessel coronary lesion was 1.18 ± 0.93 (mm), 2-vessel lesion was 1.36 ± 0.92 (mm) and 3-vessel lesion was 2.06 ± 1.25 (mm). The thickness of the femoral intima-media in patients with 1, 2 and 3 main artery disease tends to increase.

Table 7. Ratio of femoral intima-media thickness and atheroma

	Male (1)		**Female** (2)		**Total** (3)		**P** (1),(2)
	n	**%**	n	**%**	n	**%**	
Thick IMT (IMT ≥ 1.0 mm)	45	57.0	16	50.0	61	55.0	< 0.05
Atheroma/femoral (IMT ≥ 1.5 mm)	29	36.7	12	37.5	41	36.9	> 0.05

The rate of patients with thick of the intima-media layer femoral artery on ultrasound was 55.0%, of which 57.0% for male and 50.0% for female. The detection rate of femoral atheroma (with femoral IMT ≥ 1.5 mm) was 36.9%, of which 36.7% for male and 37.5% for female.

Table 8. F.IMT according to several risk factors for coronary artery disease

Risk factor of CAD	**Yes** (1)		**No** (2)		**P** (1) and (2)
	n	M ± SD (mm)	n	M ± SD (mm)	
Hypertension	65	1.71 ± 1.26	46	1.38 ± 0.89	p=0.132
History of CAD	48	1.64 ± 1.14	63	1.49 ± 1.11	p=0.015
Hyperglycemia	28	2.02 ± 1.18	83	1.42 ± 1.08	p=0.019
Hyper-totalcholesterolemia	47	1.57 ± 1.17	64	1.58 ± 1.10	p=0.532
Hypertriglyceridemia	50	1.51 ± 1.11	60	1.60 ± 1.14	p=0.66
Hyper-LDLCholesterolemia	32	1.77 ± 1.24	79	1.49 ± 1.07	p=0.25
Hypo-HDLCholesterolemia	48	1.49 ± 1.11	63	1.64 ± 1.14	p=0.511
Smoking	57	1.65 ± 1.14	54	1.49 ± 1.11	p=0.228

For a group of patients with a history of coronary artery disease and diabetes, mean femoral intima-media thickness was statistically significant compared with the group without.

3.4. The correlation between lower extremity artery damage on B-mode and Doppler ultrasound and coronary artery diasease:

Table 9. Correlation between F.IMT with age, blood pressure, glucose and blood lipids

	Age	**Blood pressure**	**Glucose**	**Total –C**	**LDL_C**	**TG**	**HDL_C**
F.IMT	r=0.319 p<0.01	r=0.351 p<0.05	r=0.404 p<0.001	r=0.205 p<0.05	r=0.170 p>0.05	r=0.035 p>0.05	r=-0.001 p>0.05

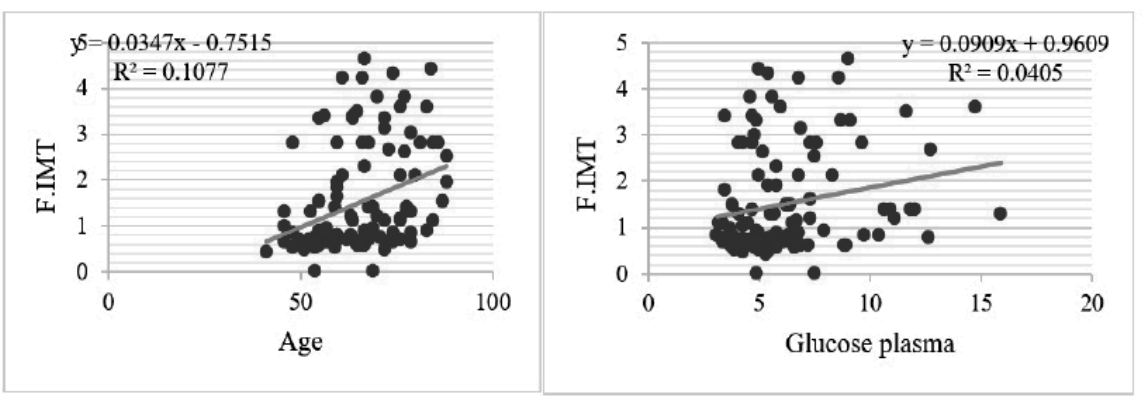

Figure 1. Correlation between F.IMT with age and plasma glucose.

There was a statistically significant and positive correlation (0.3 ≤ r < 0.5 and p < 0.01) between the thickness of the femoral intima-media with age and plasma glucose level (r = 0.404 and p < 0.001)

Table 10. Correlation between the thickness of the femoral intima-media with the number of main coronary vessel damage:

	Number of main coronary vessel	
	r	**p**
F.IMT	r=0,282	p < 0.001

Correlation between the thickness of the femoral intima-media with the number of main coronary vessel damage was a weak positive correlation and statistically significant with r = 0.282 and p < 0.001.

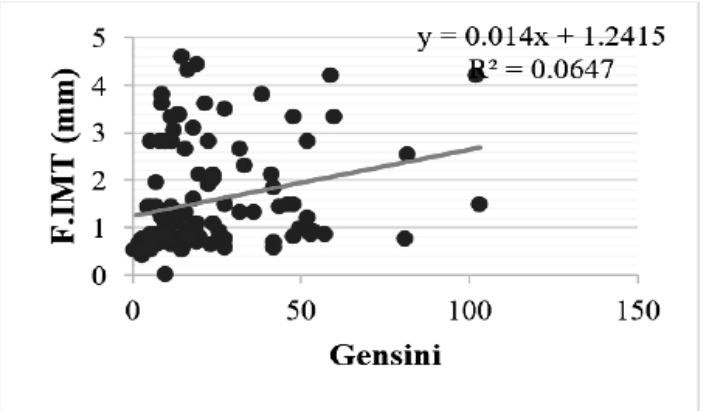

Figure 2. Correlation between F.IMT and Gensini score.

There was a weak correlation and statistically significant between the thickness of the femoral intima-media with the severity of coronary artery lesions according to the Gensini score with correlation coefficient r = 0.247 and p < 0.05, and the linear regression equation y = 0.014x + 1.2415.

4. DISCUSSION

4.1. Femoral intima-media thickness on ultrasound:

According to Depairon et al. (2000) [8], F.IMT study in 98 healthy patients (53 women and 45 men) aged 20 to 60, with no risk factor of cardiovascular diseases. F.IMT was 0.543 ± 0.0063 (mm) in women and 0.562 ± 0.074 (mm) in men, annually increase in F.IMT in women was 0.0012 (mm) and 0.0031 (mm) in men. According to Junyent M. et al. (2008) [10], studied in the intima-medina thickness of the femoral artery on 192 healthy subjects (85 men, 107 women, mean age 49 years) by ultrasound. F.IMT values were ranged from 0.50 - 1.04 (mm) in men aged 35 - 65 years and 0.40 - 0.53 (mm), F.IMT correlated strongly with age and increased annually about 0.016 (mm) in men and 0.008 (mm) in women.

F.IMT in our study was statistically significantly higher than the results of the two above authors with p < 0.001.

Compared to the study of Grozdinski (2009) on 87 patients with coronary artery diseases, the mean F.IMT was 1.46 ± 0.41 (mm) compared with the group of patients without stenosis was 0.85 ± 0.16 (mm) as well as the control group of 32 healthy subjects was 0.81 ± 0.14 (mm). This difference compared to our study is no statistically significant with p > 0.05 [9].

Table 6 showed: mean F.IMT in patients with 1-vessel coronary lesion was 1.18 ± 0.93 (mm), 2-vessel was 1.36 ± 0.92 (mm) and 3–vessel was 2.06 ± 1.25 (mm). F.IMT in patients with 1, 2 and 3 of the main vessels tended to increase and differ from statistical significance.

Lagroodi R. M. et al (2010), studied on 100 patients with coronary artery diseases divided into 4 groups: group with 1,2,3 vessel diseases and group with left main coronary lesions. Results: 1-vessel lesion group: mean F.IMT was 0.64 ± 0.11mm, 2 vessels were 0.73 ± 0.10mm; 3-vessel was 0.84 ± 0.15 and the left main lesion group was 0.85 ± 0.08 (mm). F.IMT increased gradually with the number of vessel lesions, (p <0.001) [14].

Regarding the F.IMT value, currently there is no value- approved universally on F.IMT value for each age group and gender. Many authors agree to choose the reference value (cut-off) F.IMT is 1 (mm) as Khoury Z. et al [11], Simon A. et al [19]. In this study, we defined femoral intima-media thickness when F.IMT ≥ 1 (mm) and called femoral

atherosclerosis when F.IMT ≥ 1.5 (mm). Table 7 showed that: The proportion of patients with thick layer of the inner lining of the femoral artery on ultrasound accounted for 55.0%, (male 57.0% and female 50.0%). The difference between the sexes was statistically significant with p < 0.05 and the detection rate of atherosclerosis in the femoral artery (with F.IMT ≥ 1.5 mm) was 36.9%, (male 36.7% and women 37.5%). Khoury Z. et al. (Isarel 1997) [11], which studied on 64 patients with coronary artery diseases was of similar age to our study (68.4 versus 68.84 years), the rate of patients with evidence of atherosclerosis (F.IMT thickening and atherosclerosis) was statistically significant higher than the normal coronary arteries group (77% vs 42%). This result was statistically significant higher than our study (the rate with F.IMT thickness was 55% with p < 0.01). This may be because atherosclerosis usually occurs earlier in the Western countries, or the author's study subjects had a higher incidence of diabetes and metabolic syndrome: two risk factors strongly promote the rapid development of atherosclerosis.

According to Simon A. et al [19], the femoral and carotid intima-media thickness reflects the overall risk of atherosclerosis, many epidemiological data suggested that F.IMT ≥ 1mm was related to an increased risk of myocardial infarction or stroke. There was a strong correlation between F.IMT and traditional cardiovascular risk factors and new risk cardiovascular factors. Many evidence confirms that the increase in the thickness of the intima-media of the femoral and carotid arteries is a strong indicator for the prediction of cardiovascular events (the risk index increases by 2-6 times).

4.2. F.IMT and cardiovascular risk factors

Table 9 showed that: in patients with hypertension, the mean F.IMT was 1.71 ± 1.26 (mm), with no statistically significant difference compared to the group without hypertension. Grozdinski (2009), in a group of 74 patients with coronary artery lesion on angiography, 93.2% was hypertension (temporarily considered as patients with hypertension). The average thickness of the femoral intima-media was 1.46 ± 0.41 (mm). This difference was not statistically significant compared with our study [9].

Patients with diabetes have mean F.IMT was 2.02 ± 1.18 (mm), compared with people without diabetes, F.IMT was 1.42 ± 1.08 (mm). There was a statistically significant difference with p < 0.05.

Correlation of F.IMT with age

Table 9 showed: The correlation between age and F.IMT: There was positive, statistically significant correlation (0.3 ≤ r < 0.5 and p < 0.01) between the intima-media femoral arteries with age. This result was similar to some other authors: Depairon et al (2000) [8], Junyent M et al (2008) [10]. Lugwig et al. (2003) [6] showed that femoral intima-media thickness had a clear correlation with age, diabetes, smoking, and several other risk factors.

Correlation of F.IMT with systolic blood pressure

There was a moderately significant correlation between maximum blood pressure and F.IMT on ultrasound (0.3 ≤ r < 0.5 and p> 0.05). This result was similar to the study of Kirhmaer et al. (2011) [13], Lekakis et al (2005) [15].

Correlation of F.IMT with lipid profiles

Albeit some studies outlined that lipid profile, especially LDL-C and HDL-C, related to the thickness of femoral arteries some studies found a moderate correlation between them [11]. In our study, we did not find out this correlation after adjustment for other factors.

4.3. Correlation of lower extremity artery lesions on B-mode and Doppler ultrasound with coronary artery diseases:

Table 10 showed a slight correlation but statistically significant between F.IMT and the number of coronary artery diseases (with r = 0.282 and p <0.001 and y = 0.3069x + 0.8404). According to Sosnowski et al studied on 410 patients with coronary artery diseases showed that F.IMT was an independent risk factor that predicted lesions to coronary arteries, whereas atherosclerosis femoral artery was often associated to multiple coronary artery diseases [20].

The severity of coronary artery diseases according to the Gensini score:

There was a negative, statistically significant correlation between the femoral intima-media thickness and the severity of coronary artery diseases on the Gensini score (r = 0.247 and p <0.05, and y = 0.014x + 1.2415).

Lekakis et al [15] studied on 202 patients with coronary artery diseases, multivariate regression analysis showed that F.IMT abnormality was strongly correlated with coronary artery lesions on Gensini score, age and glucose plasma level. The author concludes that patients with higher F.IMT are more likely to be associated with multivessel coronary artery diseases and have a higher incidence of coronary artery events or stroke. Lugwig et al [16] have the same conclusion as Lekakis, and

furthermore, treatment to slow progression or degeneration of the femoral intima-media thickness reduces significantly the cardiovascular events. Doppler ultrasound is a non-invasive, popular, reliable, and an easy-to-apply technique to monitor changes in arterial intima-media thickness.

5. CONCLUSION

5.1. Lesions on the lower extremity artery on B mode and Doppler ultrasound:

- Femoral intima-media thickness (F.IMT) was 1.56 ± 1.10 mm, (male was 1.59 ± 1.19 mm, female was 1.57 ± 1.23mm, p > 0.05).

- The rate of F.IMT thick (≥ 1.0 mm) was 55.0%, (male was 57.0% and female was 55%, p < 0.05).

- The rate of femoral atherosclerosis (F.IMT ≥ 1.5 mm) was 36.9%, of which 36.7% for male and 37.5% for female, (p > 0.05).

5.2. Correlation between F.IMT and severity of coronary artery lesions:

- There was a positive, statistically significant correlation (0.3 ≤ r < 0.5 and p < 0.01) between F.IMT and age, maximum blood pressure and plasma glucose.

- There was a positive, statistically significant correlation between F.IMT and Gensini score with r = 0.247 and p < 0.05, and the linear regression equation y = 0.014x + 1.2415.

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