Mean Right and Left Carotid Intima-Media Thickness Measures in Cases with/without Coronary Artery Disease

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Abstract- One of the important factors which should be considered in (Coronary artery disease) CAD cases is increased carotid intima-media thickness (IMT) which has been considered to be associated with coronary artery disease severity and cardiovascular events. The goal of this study was to compare risk factors and carotid IMT in cases with CAD and healthy subjects and to determine the association between severity of CAD and IMT. In this case-control study, 250 proved CAD cases and 250 healthy ones were enrolled. Ultrasound evaluation of carotid IMT Ultrasound quantification of the right and left carotid IMTs was obtained. Demographic characteristics (age and sex), risk factors (presence of diabetes, hyperlipidemia (HLP), hypertension (HTN) and smoking) were recorded for all participants. Presence of diabetes, HTN, HLP and mean age was significantly higher in patients than controls. There was positive correlation between IMTs and advancing CAD (for right IMT, rho=0.34, $P<0.001$, for IMT rho=0.47, $P<0.001$). Sex, HTN, HLP, right and left IMT measures were independent predictors of CAD. The best cutoff point for right IMT to differentiate patients from controls was 0.82 with sensitivity and specificity of 70% and 50% (AUC=0.70, $P<0.001$). The best cutoff point for left IMT to differentiate patients from controls was 0.85 with sensitivity and specificity of 80% and 55% (AUC=0.70, $P<0.001$). Carotid IMT increase should be considered as a surrogate factor for CAD.

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Keywords: Coronary artery disease; Intima-media thickness; Risk factor

Introduction

Coronary artery disease (CAD) is one of the main causes of death all over the world. Different factors such as smoking, hypertension, diabetes, fibrinogen, and low-density lipoprotein cholesterol (LDL cholesterol) is accepted risk factors for CAD (1). Among different surrogates, increased carotid intima-media thickness (IMT) has been considered to be associated with coronary artery disease severity and cardiovascular events (2).

Carotid IMTis a marker of subclinical atherosclerosis. Investigators evaluated effects of different risk factors on IMT and also the effects of the risk factors modifications on thickness of the intima-media (3,4). They found that IMT would increase with age, sex, hypertension, diabetes mellitus, hyperlipidaemia, and other factors that are associated with CAD (5-7).

IMT evaluation has been recommended as a screening tool for cardiovascular occurrence especially in high risk population such as diabetic cases, elderly people, and patients with hyperlipidemia, hypertension and smokers (4-8) but there is not agreement to measure this item as screening tool of coronary diseases in the normal population (9). On the other hand, IMT has been considered to show severity of CAD.

In a previous study, Kablak-Ziembicka *et al.,* reported higher mean IMT in patients with CAD in comparison with healthy controls. They also found that more advanced CAD was associated with higher IMT (3 versus 2 or one vessel) (10).

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As CAD is a one of the most common causes of death all over the worlds as well as in Iran, and there are limited studies evaluating IMT in CAD and healthy controls, we designed this study was to compare risk factors and carotid IMT in cases with CAD and healthy subjects and to determine association between severity of CAD and IMT.

Materials and Methods

In this case-control study which conducted in the radiology department of Zanjan university of medical sciences between March2012 and March 2013.

250 proved CAD cases and 250 healthy ones (who suspected to have coronary disease) according to coronary angiographies were enrolled.

Demographic characteristics (age and sex), risk factors (presence of diabetes, hyperlipidemia, hypertension and smoking) were recorded for all participants.

All enrolled cases were asked to fill informed consent forms before study entrance.

Ultrasound evaluation of carotid IMT Ultrasound quantification of the right and left carotid IMTs were obtained with high resolution B mode by means of 7.5-15 MHz linear array transducer (SIEMENS, G50, Germany). All scans were obtained by a radiologist who was blinded to the patients' clinical and angiographic characteristics.

During examination, patients were in the supine position with the neck extended, and the chin turned away from the side being examined.

The maximum IMT was measured at the near and far walls of the common carotid artery. For each subject, the mean right and left IMTs were calculated as the average of all mean IMT measurements.

All data were analyzed using SPSS software version 18.0 (SPSS Inc., Chicago, IL, USA). Data were presented as mean ± SD for continuous or frequencies for categorical variables.

Spearman correlation coefficient calculated to determine the association between IMT and advancing CAD.

Multiple regression analysis was used to calculate the predictive value of risk factors for the right and left IMTs. Logistic regression analysis applied to determine if risk factors and IMT are predictors for CAD. ROC curve was used to determine optimal cut-off values of right and left IMTs. Area under the Curve (AUC) calculated.

P-value less than 0.05 was considered significant.

Results

Five hundred cases enrolled in this study. In patient group, One vessel CAD was diagnosed in 111(44.4%), two vessel CAD in 81(32.4%) and three vessel CAD in 58(23.2%). Mean age was higher in cases with three vessels CAD (Table 1).

Mean right and left IMTs were significant higher in patient groups than normal group (Table 2).

Table 1. Demographic characteristics of the participant

	Normal	One vessel CAD	two vessel CAD	three vessel CAD	*P.* value
Age (year)	57.2±10.9	60.1±10.3	62.5±11.9	62.6±12	<0.001
Sex (M/F)	(105/145)	(85/26)	(56/25)	(41/17)	<0.001
Diabetes(yes/no)	(24/ 226)	(13/ 98)	(6/ 75)	(17/ 41)	<0.001
HTN(yes/no)	(120/130)	(53/58)	(39/42)	(34/24)	0.5
HLP (yes/no)	(131/119)	(105/6)	(75/6)	(55/3)	<0.001
Smoking (yes/no)	(38/212)	(34/77)	(22/59)	(13/45)	<0.001

Table 2. Mean right and left IMTs in different groups

	Normal	One vessel CAD	two vessel CAD	three vessel CAD	*P.* value
Right IMT(m)	0.84±0.24	1±0.32	1.1±0.3	1±0.3	<0.001
Left IMT(m)	0.85±0.24	1.13±0.29	1.13±0.28	1.15±0.21	<0.001

Mean right and left IMTs were significant higher in patient groups than normal group (Table 2).

Mean right and left IMT measures were significantly higher in all enrolled participants with and without HLP (Table 3).

There was positive correlation between IMTs and advancing CAD (for right IMT, rho=0.34, $P<0.001$, for IMT rho=0.47, $P<0.001$). Sex, HTN, HLP, right and left IMT measures were independent predictors of CAD.

Sex, age and HLP were independent predictors of right IMT measure (Table 5).

HLP was the only independent predictor of left IMT measure (Table 6).

The best cutoff point for right IMT to differentiate patients from controls was 0.82 with sensitivity and specificity of 70% and 50% (AUC=0.70, $P<0.001$) (Figure 1).

The best cut-off point for left IMT to differentiate patients from controls was 0.85 with sensitivity and specificity of 80% and 55% (AUC=0.70, $P<0.001$) (Figure 2).

Table 3. Mean right and left IMTs in different groups with different risk factors

	Yes	No	*P.* value
Diabetes			
Right IMT(m)	0.95±0.29	0.95±0.3	0.9
Left IMT(m)	1±0.26	1±0.44	0.6
HTN			
Right IMT(m)	0.94±0.29	0.96±0.31	0.4
Left IMT(m)	0.99±0.29	1±0.53	0.5
HLP			
Right IMT(m)	0.97±0.31	0.88±0.26	0.002
Left IMT(m)	1±0.47	0.9±0.27	0.001
Smoking			
Right IMT(m)	0.97±0.32	0.94±0.29	0.4
Left IMT(m)	1±0.29	0.99±0.45	0.1

Table 4. Logestic regression analysis for defining predictors of CAD

	OR	*P.* value
Sex	0.27	<0.001
Age	1	0.1
Right IMT	12.1	<0.001
Left IMT	11.3	<0.001
Diabetes	0.58	0.14
Hypertension	0.43	0.002
Hyperlipidemia	0.06	<0.001
Smoking	0.54	0.07

Table 5. Linear regression analysis between right IMT and other variables

	B coefficient	*P.* value
Sex	-0.15	0.001
Age	0.09	0.04
Diabetes	0.014	0.7
Hypertension	0.009	0.8
Hyperlipidemia	-0.09	0.03
Smoking	0.01	0.8

Table 6. linear regression analysis between left IMT and other variables

	B coefficient	*P.* value
Sex	-0.03	0.4
Age	0.07	0.1
Diabetes	-0.01	0.7
Hypertension	0.007	0.8
Hyperlipidemia	-0.12	0.006
Smoking	-0.05	0.3

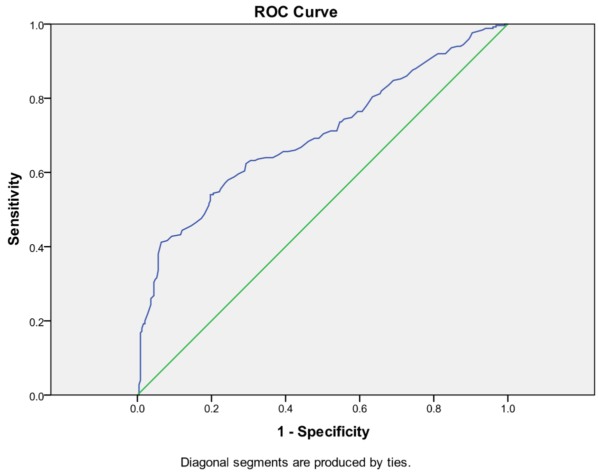

Figure 1. ROC curve for the best cut-off point for the right IMT

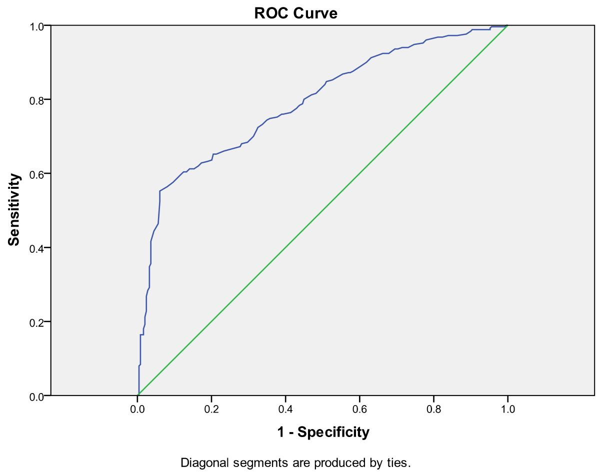

Figure 2. ROC curve of the best cutoff point for left IMT

Discussion

The results of current study showed that mean right and left IMTs were significantly higher in CAD patients than controls and a significant correlation between IMT and advancing CAD (for right IMT, rho=0.34, $P<0.001$, for IMT rho=0.47, $P<0.001$) was investigated.

The results also showed that mean right and left IMTs were significantly different in cases with and without hyperlipidemia but meant IMTs were not significant different in cases with and without other risk factors.

These findings are compatible with Kablak-Ziembicka *et al.*, findings. In their study, patients with CAD had significantly higher IMT than participants without CAD (10).

Mean IMT were significantly higher in patients with three-vessel CAD than other two groups (one and two vessels).

In another study, Crouse *et al*., reported a strong association between CAD and mean IMT of carotid arteries (11).

Bots *et al*., followed 7983 patients aged 55 years and over for 4.6 years. They observed 194 new myocardial infarctions in the study group. They had evaluated carotid IMT in all participants at the study entrance and found that mean carotid IMTs were significantly higher in MI cases than others. They also investigated a positive correlation between carotid IMT and the incidence of myocardial infarction (12).

Evaluating carotid IMTs in over 5800 patients (≥ 65 years of age), O'Leary *et al.,* reported association between increased carotid IMT and an increased risk of myocardial infarction and stroke in cases with negative history of cardiovascular disease (13).

Previous studies showed that age, sex, hypertension, diabetes mellitus, hyperlipidaemia and hypertension are among risk factors that influence carotid IMT (4,5,7). Our results show that age, sex, hyperlipidemias are independent predictors of right IMT while only hyperlipidemia is the independent predictor of left IMT.

We also found that sex, HTN, HLP and values of right and left IMTs are among independent predictors of developing CAD. CAD remains one the most causes of death in both developing and developed countries. It is prevalence increases with the increase of age. For instance, prevalence of CAD is 2.8-fold higher in adults aged 65–74 years than cases aged 45–64 years (14). Different risk factors such as HTN, HLP, smoking and diabetes are known risk factors of developing CAD. Risk factor analysis can help the physicians to identify cases that are at risk of CAD and consider plans to modify risk factors.

As the sensitivity and specificity of treadmill testing or echocardiography are limited, IMT measurements of the carotid arteries will be helpful in evaluating the status of the cases with cardiovascular risk factors. Increased IMT will guide the practitioner to coronary angiography and tight control of risk factors (15,16).

However, it should be considered that only IMT value of carotid arteries could not predict the extent of CAD. May be IMT measurement could help more attention to cases without previous CAD history as a screening tool for patients with suspected CAD.

Conclusion: Carotid IMT increase should be considered as a surrogate factor for CAD.

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