Shiraz E-Med J. 2015 May; 16(5): e27906. DOI: 10.17795/semj27906

Published online 2015 May 10. **Research Article**

Predictors of Common Carotid Artery Intima-Media Thickness and Atherosclerosis in a Sample of Iranian General Population

Kamran Bagheri Lankarani [1]; Fariborz Ghaffarpasand [2]; Mojtaba Mahmoodi [1]; Maryam Dehghankhalili [1,*]; Behnam Honarvar [1]; Mehrzad Lotfi [3]; Nima Zamiri [1]; Sayed Taghi Heydari [4]; Mohammad Kazem Fallahzadeh [1]; Najmeh Maharlouei [1]; Mohammad Saeid Khaksar [5]; Bita Geramizadeh [6]

[1]Health Policy Research Centre, Shiraz University of Medical Sciences, Shiraz, IR Iran
[2]Neuroscience Research Centre, Shiraz University of Medical Sciences, Shiraz, IR Iran
[3]Department of Radiology, Shiraz University of Medical Sciences, Shiraz, IR Iran
[4]Department of Biostatistics, Jahrom University of Medical Sciences, Jahrom, IR Iran
[5]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, IR Iran
[6]Department of Pathology, Transplant Research Centre, Shiraz University of Medical Sciences, Shiraz, IR Iran

*Corresponding Author: Maryam Dehghankhalili, Health Policy Research Centre, Shiraz University of Medical Sciences, Shiraz, IR Iran. Tel: +98-936-9799535, Fax: + 98-7132309615, E-mail: Maryam_dhkh@yahoo.com

Received: February 12, 2015; **Accepted:** February 28, 2015

Background: Measurement of common carotid artery intima–media thickness (IMT) is considered a safe, inexpensive, precise and reproducible measure of atherosclerosis. It is also considered an early predictor of vascular events such as cerebrovascular and cardiovascular complications.

Objectives: This study aimed to determine the predictors of common carotid Intima-Media Thickness (IMT) and cardiovascular risk factors in a sample of Iranian general population.

Patients and Methods: This cross-sectional study was performed on a randomly selected sample of Iranian general population in Shiraz, southern Iran, during a 10-month period from November 2010 to September 2011. All patients underwent anthropometric and blood pressure measurements and medical history assessment and physical examination were also performed. Laboratory measurements included Fasting Blood Glucose (FBS), lipid profile, Complete Blood Count (CBC) and thyroid hormones. Moreover, IMT was measured in the subjects with a cut-off point of 0.8 mm and its correlation with other risk factors was assessed.

Results: From a total of 777 eligible subjects included in the study, 326 cases (42%) were male and 451 (58%) were female with the mean age of 42.64 ± 13.89 (ranging from 18 to 88) years. Overall, 78 (10.1%) subjects had hypertension, 51 (6.5%) were diabetic and 158 (20.3%) had metabolic syndrome. Moreover, IMT was found to be normal in 605 (77.9%) subjects while 172 (22.1%) subjects had thick IMT. Patients with IMT thicker than 0.8 mm were significantly older ($P < 0.001$) and had a higher prevalence of hypertension ($P < 0.001$), Diabetes Mellitus (DM) ($P = 0.016$), smoking ($P = 0.002$), higher levels of Triglyceride (TG) ($P = 0.022$), higher Body Mass Index (BMI) ($P = 0.005$) and larger waist circumference ($P < 0.001$). Thicker IMT was associated with higher risk of metabolic syndrome ($P = 0.008$). Women had also a higher prevalence of thick IMT compared to men (50.6% vs. 49.4%; $P = 0.027$).

Conclusions: The prevalence rates of cardiovascular risk factors as well as metabolic syndrome are relatively high in our region. Intima-media thickness is affected by age, hypertension, DM, smoking, BMI, waist circumference and TG levels and is an appropriate predictor of atherosclerosis. Appropriate policies and actions should be undertaken to prevent the cardiovascular events in our regions.

Keywords: Carotid Intima-Media Thickness; Carotid Artery, Common; Cardiovascular diseases; Iran

1. Background

The common carotid arteries are considered among the most susceptible vessels to develop early and progressive atherosclerosis in the presence of cardiovascular risk factors such as smoking, Diabetes Mellitus (DM), dyslipidemia and hypertension (1, 2). The characteristics of changes in arterial wall include intimal thickening and endothelial dysfunction, which occur during a long period of time. Currently, several markers and noninvasive methods such as thickening as well as stiffening of arterial wall, endothelial dysfunction and calcification of the coronary artery are available for early arterial wall alteration screening (1). Measurement of common carotid artery Intima-Media Thickness (IMT) using B-mode ultrasound is considered a safe, inexpensive, precise and reproducible measure of atherosclerosis (3-5). It is also considered an early predictor of vascular events, such as cerebrovascular and cardiovascular complications (6, 7).

Intima-media thickness is considered a reliable and available marker of atherosclerosis and its clinical course

(8). It has been indicated that IMT is increased in patients suffering from ischemic heart disease (9). It has also been demonstrated that IMT could serve as an independent risk factor for stroke or myocardial infarction (10). These characteristics have led to increase the use of IMT in clinical research for evaluating the effect of risk factor modifications or to determine the role of new risk factors for cardiovascular diseases (11). According to the high predictive value of IMT in determining the cardiovascular diseases' complications, it can also be concluded that IMT would be used in cardiovascular risk stratification of asymptomatic patients (12).

2. Objectives

In this regards, we performed this population-based study to determine the predictors of common carotid IMT and cardiovascular risk factors in a sample of Iranian general population.

3. Patients and Methods

3.1. Study Population

This cross-sectional study was performed in Shiraz, southern Iran, during a 10-month period from November 2010 to September 2011 including a randomly selected sample of Iranian general population. This study was a part of health survey, which was performed in Shiraz during this time period. Fars Province is located in the south of Iran and cover 122,483 sq km with a population of just over 5.5 million mainly comprising Iranians (73.2%). Shiraz is the capital and main city of Fars Province with an estimated population of 1.7 million according to the recent national census. The sample clustering method was used to obtain a representative sample of Shiraz general population. Participants were randomly drawn from all over the Shiraz City consisting of 7 areas according to municipality regions with 1,711,186 inhabitants based on their Zip Codes. All those randomly selected inhabitants who were older than 20 years of age and administered through phone were included in the study. We excluded pregnant women or those who had delivered within six months prior to study. Non-Iranians were also excluded. The study protocol was approved by Institutional Review Board (IRB) and the research ethics committee of health policy research center affiliated to Shiraz University of Medical Sciences. All the participants gave their informed written consents.

3.2. Study Protocol

Participants were selected randomly based on their Zip Codes registered in Shiraz Central Post Office. Invitations for participation describing the study protocol were posted to selected residential houses. Through the invitation letter, the inhabitants older than 20 years of age were asked to call the clinic for registration. All the participants were also asked to attend the clinic after an overnight fasting. After administration, 1000 participants were introduced to the health survey clinic. A team of healthcare workers (two physicians and two nurses) were settled in the health survey clinic in order to perform interview and physical examinations. Each participant was visited by the team separately and filled the forms under the supervision of the team members. We used a data gathering form including 4 separate parts in this survey. Form no. 1 contained general information including the number of family members, their age and sex, and the nutritional status. Levels of education and occupation of the subjects, and marital status and smoking habit were also sought. Form no. 2 contained information on nutritional status and habits of each participant. Form no. 3 contained questions about medical history and general physical state and the findings of physical examinations by physicians. Form no. 4 contained results of laboratory tests being performed for each individual.

A face-to-face interview was carried out by two physicians separately (one male physician and one female physician based on the gender of participants). The anthropometric measurements were performed by two nurses and were recorded into forms. Physical examinations including body height, weight, waist circumference, hip circumference, Waist-to-Hip Ratio (WHR), liver span, Body Mass Index (BMI), heart rate and blood pressure were also measured by the physicians. Intravenous blood samples were drowned from fasting subjects to measure Fasting Blood Sugar (FBS), Triglyceride (TG), cholesterol, Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL) and Thyroid Stimulating Hormone (TSH). Also, Complete Blood Count (CBC) was determined using the autoanalysis method. Diabetes mellitus was defined according to the American Diabetes Association criteria based on FBS > 126 mg/dL (13). The hypertension was defined according to 7^{th} Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7 report) (14).

3.3. Carotid Ultrasonography

Carotid Doppler ultrasonography was performed and the sonograms were interpreted by an experienced radiologist in a single accredited laboratory at our institution, Color Doppler Sonography (CDS) of both carotid vessels were done by LOGIC-7 ultrasound unit in Nemazee Hospital. All images were obtained in accordance with an established laboratory protocol. All patients underwent gray-scale as well as color and spectral Doppler imaging. Also, IMT of right and left Common Carotid Arteries (CCA) was assessed for each patient according to the formula (0.009 × age) + 0.116 to determine the age-specific cut-off point. We used the cut-off point of 0.8 mm for abnormality.

3.4. Statistical Analysis

Statistical analyses were performed using the SPSS software, version 16.0 (SPSS Inc. Chicago, Ill., USA). The chi-square test was used to compare the proportions between those with normal and abnormal IMT. An independent t-test was used to compare the parametric data between the two groups. The results are expressed as Mean ± SD and proportions as appropriated. A two-tailed P value < 0.05 was considered statistically significant.

4. Results

4.1. Demographics and Socioeconomic Status

From a total of 777 eligible subjects included in the study, 326 cases (42%) were men and 451 (58%) were women with the mean age of 42.64 ± 13.89 (ranging from 18 to 88) years. Most of the participants (26.1%) were categorized as middle aged (40 - 49 years of age). The demographic characteristics and socioeconomic status of the participants are summarized in Table 1. Most of the participants (58.9%) were categorized as moderate income while 339 (43.7%) had educated ≤ 12 years. Also, 653 subjects (84%) were married and 124 (16%) were single. The mean number of family members was found to be 4.1 subjects.

4.2. Anthropometric Measurements

Table 2 demonstrates the anthropometric characteristics of 777 subjects participated in the health survey. The mean BMI was found to be 26.1 ± 4.3 kg/m^2. Most of the participants (39.6%) were overweight and 15.7% were obese while 38.7% of them were normal. Women had significantly lower height (P < 0.001), weight (P < 0.001) and waist circumference (P < 0.001) but higher BMI (P < 0.001) compared to men. Age was positively correlated with BMI in both men (r = 0.175, P = 0.002) and women (r = 0.333, P < 0.001).

Table 1. Demographic Characteristics and Socioeconomic Status of 777 Subjects Participated in the Health Survey [a]

Variables	Values [a]
Age, y	
18 – 29	163 (21.0)
30 – 39	157 (20.2)
40 – 49	203 (26.1)
50 – 59	163 (21.0)
≥ 60	91 (11.7)
Gender	
Male	326 (42)
Female	451 (58)
Income	
Low (< 400 USD/mo)	274 (35.2)
Mid (400 - 800 USD/mo)	354 (45.6)
Moderate (800 -1000 USD/mo)	103 (13.3)
High (≥ 1000 USD/mo)	46 (5.9)
Years of education	
Illiterate	51 (6.5)
≤ 12	470 (60.5)
13 - 16	173 (22.3)
17 – 19	42 (5.4)
Marital status	
Married	653 (84)
Single	124 (16)
Family members	
One	25 (3.2)
Two – Five	628 (80.8)
> Five	124 (16)

[a] Data are presented as No. (%).

Table 2. Anthropometric Measurements of 777 Subjects Participated in the Health Survey [a]

	Male (n = 326)	Female (n = 451)	Total (n = 777)
Height, cm	172.67 ± 8.02	157.71 ± 6.93	163.9 ± 13.8
Weight, kg	74.54 ± 12.12	66.71 ± 11.42	70.1 ± 12.3
Waist circumference, cm	92.46 ± 9.62	86.68 ± 11.36	89.1 ± 11.3
Hip circumference, cm	102.01 ± 6.72	102.59 ± 10.38	102.3 ± 9.1
Body mass index (kg/m^2)	25.01 ± 3.74	26.87 ± 4.63	26.1 ± 4.3
Underweight	14 (4.3)	9 (2.0)	23 (3.0)
Normal	152 (46.6)	149 (33.0)	301 (38.7)
Overweight	126 (38.7)	182 (40.4)	308 (39.6)
Obese	31 (9.5)	91 (20.2)	122 (15.7)
Severely Obese	3 (0.9)	20 (4.4)	23 (3.0)

[a] Data are presented as mean ± SD or No. (%).

4.3. Smoking Habits

Of the population studied, 148 cases (19.3%) were smokers among which 89 (11.5%) were cigarette smokers and 59 (7.8%) were water-pipe smokers. Among the participants, 30 cases (3.9%) had quit smoking for at least 1 year. The mean pack/year was found to be 12.3 ± 3.6 in our series with 52 (6.7%) heavy smokers (> 20 pack/year). Routine alcoholic beverage consumption was reported by 29 individuals (3.8%) while 58 (7.4%) consumed these beverages intermittently. Opium and its products were used by 26 cases (3.3%) through ingestion or inhalation. None of the participants were intravenous drug abusers.

4.4. Diabetes Mellitus and Hypertension

The mean systolic and diastolic blood pressures were 115.1 ± 16.2 and 75.2 ± 9.8 mmHg, respectively. Overall, 459 individuals (59.1%) were normotensive while 240 (30.9%) had prehypertension, 62 (8.0%) had stage I hypertension and 16 (2.1%) had stage II hypertension. Moreover, 78 subjects (10.1%) had hypertension out of which 59 (7.6%) were aware of their disease and consumed antihypertensive drugs. The prevalence of hypertension was significantly higher among men (11.9% vs. 8.7%; P = 0.032). The mean FBS was found to be 92.9 ± 29.1 mg/dL. Out of 777 participants, 578 (74.4%) were normal, 148 (19.1%) had impaired glucose tolerance and 51 (6.5%) were diabetic. However, 46 cases (5.9%) were aware of their disease and only 35 (4.5%) consumed glucose lowering agents for plasma glucose control.

4.5. Lipid Profile

The lipid profile of 777 subjects participated in this survey is summarized in Table 3. The mean serum level of cholesterol (P < 0.001) was significantly higher in women compared to men and the serum level of HDL (P < 0.001) was also significantly higher in women (P < 0.001). The prevalence of hypercholesterolemia was also higher among women (P = 0.008) while they had lower prevalence of low HDL (P = 0.001). Taking all these findings together, 158 cases (20.3%) were diagnosed to have metabolic syndrome. Patients with the metabolic syndrome were significantly older compared to healthy subjects (52.2 ± 13.3 vs. 40.7 ± 13.2; P < 0.001).

4.6. Common Carotid Artery Intima-Media Thickness

Overall, the IMT was found to be normal in 605 cases (77.9%) while 172 (22.1%) had IMT thicker than 0.8 mm. In the same way, 61 (7.8%) patients had carotid artery plaques. Patients with IMT thicker than 0.8 mm were significantly older compared to normal subjects (51.9 ± 13.5 vs. 40.2 ± 12.7; P < 0.001). Table 4 compares cardiovascular risk factors among those with IMT > 0.8 mm and normal IMT. Patients with thick IMT were significantly older (P < 0.001) and had a higher prevalence of hypertension (P < 0.001), DM (P = 0.016) and smoking (P = 0.002). In the same way patients with thick IMT had significantly higher levels of TG (P = 0.022), higher BMI (26.9 ± 4.4 vs. 25.4 ± 4.5 kg/m^2; P = 0.005) and larger waist circumference (91.9 ± 10.8 vs. 88.1 ± 11.7 cm; P < 0.001). Thicker IMT was associated with a higher risk of the metabolic syndrome (P = 0.008). Women had also the higher prevalence of thick IMT compared to men (50.6% vs. 49.4%; P = 0.027). Serum levels of LDL and HDL were comparable between two study groups. We also tried to investigate a cut-off value for age in which the IMT increases beyond 0.8 cm. We found that 45 years of age is an appropriate cut-off value with sensitivity and specificity of 72.1% (CI 95%: 64.8 - 78.7) and 67.7% (CI 95%: 63.7 - 71.6), respectively and the area under curve (AUC) of 0.744 (CI 95%: 65.8 - 82.6).

Table 3. Lipid Profile of 777 Subjects Participated in the Health Survey [a]

	Male (n = 326)	Female (n = 451)	Total (n = 777)
Cholesterol, mg/dL	187.3 ± 42.6	137.8 ± 72.1	191.1 ± 42.6
Normal	225 (69.1)	272 (60.3)	497 (63.9)
High	101 (30.9)	179 (39.7)	280 (36.1)
Triglyceride, mg/dL	145.2 ± 84.3	137.8 ± 72.1	140.8 ± 77.4
Normal	224 (68.8)	314 (75.6)	538 (69.2)
High	102 (31.2)	137 (24.4)	239 (30.8)
LDL, mg/dL	105.9 ± 33.3	107.4 ± 35.2	106.8 ± 34.4
Normal	306 (93.8)	417 (92.4)	723 (93.1)
High	20 (6.2)	34 (7.6)	54 (6.9)
HDL, mg/dL	47.7 ± 9.2	52.7 ± 11.4	50.6 ± 10.8
Normal	272 (83.4)	412 (91.4)	684 (88.3)
Low	54 (16.6)	39 (8.6)	93 (11.7)

[a] Data are presented as mean ± SD or No. (%).

Table 4. Cardiovascular Risk Factors According to the Intima-Media Thickness (IMT) in 777 Subjects [a]

	IMT > 0.8 (n = 172)	IMT < 0.8 (n = 605)	P Value
Age, y			< 0.001
18 - 29	14 (8.1)	144 (23.9)	
30 – 39	18 (4.7)	150 (24.8)	
40 – 49	41 (23.8)	163 (27.0)	
50 – 59	60 (34.9)	99 (16.5)	
≥ 60	49 (28.5)	49 (7.8)	
Gender			0.027
Male	85 (49.4)	240 (39.7)	
Female	87 (50.6)	365 (60.3)	
High Cholesterol	62 (36.1)	204 (33.7)	0.127
High Triglyceride	73 (42.4)	197 (32.6)	0.022
High LDL	13 (7.4)	40 (6.7)	0.865
Low HDL, mg/dL	62 (36.1)	195 (32.3)	0.403
Hypertension	59 (34.3)	98 (16.3)	< 0.001
DM	19 (11.1)	34 (5.6)	0.016
High Waist Circumference	64 (37.2)	196 (32.4)	0.269
BMI > 25 kg/m^2	121 (70.4)	331 (54.8)	0.008
Metabolic Syndrome	46 (26.7)	105 (17.4)	0.008
Smoking	53 (30.8)	95 (15.7)	0.002

[a] Abbreviations: BMI, Body mass index; DM, Diabetes Mellitus; HDL, High density lipoprotein; IMT, Intima-media thickness; LDL, Low density lipoprotein.

5. Discussion

Common carotid IMT has been reported as a precise measure of atherosclerosis (2, 15), which is directly associated with progression and extend of organ damage in patients with cardiovascular disorders (16-18). Increased IMT is an indicator of brain white matter lacunar infarctions (19), atherosclerosis (20) and calcification (21) of the coronary arteries. Linhart and coworkers demonstrated that increased IMT is associated with increased left ventricular dysfunction in asymptomatic men who had ischemic heart disease risk factors (22). A relationship has also been reported between microabuminuria and IMT regardless of diabetes (23). Taking all these together, it can be concluded that IMT is not only the indicator of atherosclerosis but also a precise indicator of end organ damage secondary to arterial wall damage. In this regards, we performed this cross-sectional study to determine the significance of IMT for cardiovascular risk stratification in sample of Iranian general population. We found that the frequency rates of increased common carotid artery IMT and atherosclerotic plaque in Shiraz were 22.1% and 7.8%, respectively. Patients with thick IMT had significantly higher prevalence of hypertension, DM and smoking. They had also higher age, BMI, waist circumference and serum levels of TG resulting in a higher prevalence of metabolic syndrome compared to those with normal IMT. This demonstrates that age, hypertension, DM, smoking, BMI and waist circumference are the most important risk factors for atherosclerosis in our population while lipid profile is of less importance. These findings are in accordance with previous reports (20-23).

Aminbakhsh and Mancini demonstrated that the risk of cardiovascular disease increased significantly by increasing the IMT by 0.034 mm or more (approximately 10 times the normal increase per year) (24). Increased IMT is also associated with increased risk of peripheral arterial occlusive diseases (25), and abdominal aortic aneurysm (26). Vice versa, it has been shown that those with peripheral arterial occlusive disorders who have increased IMT, have higher risk of cardiovascular complications (27). Schreiner and coworkers (27) demonstrated that the relationship between increased IMT and cardiovascular complications is mostly prominent in those with intermittent claudication. Only one study by Adams and colleagues challenged the predictive value of IMT as an indicator of severity and extend of coronary artery disease (28).

One of the striking findings of this survey was the high frequency of overweight in our series. Obesity was also reported in 15.7% of the population, which is significantly higher compared to previous Iranian surveys (29). Tahaghoghi and Massarrat (29) detected obesity in 11% and 6.2% of males residing in urban and rural areas, respectively, and in 27.6% and 15.6% of females residing in urban and rural areas, respectively. However, the prev-

alence of obesity in Shiraz is 9.5% in men and 20.2% in women. Overall the BMI is significantly higher in women compared to men probably because of lower height in Iranian women descendant. This finding becomes more important by taking into consideration the high prevalence of dyslipidemia and hypertension indicating the high prevalence of metabolic syndrome in our region, which was 20.3%. The prevalence of metabolic syndrome has been reported to be 28% in USA and < 10% in France (30). Comparable with previous reports, the prevalence increased with age and was more common among women. The prevalence of metabolic syndrome is relatively high in our region, which is an indicator of industrialization. We also found that the cut-off value beyond which the IMT increases beyond the 0.8 cm is 45 years in our population. This means that we should perform screening programs in middle age population regarding the IMT in order to investigate the cardiovascular diseases progression and risk.

We note some limitations to this study. First, the study population was slightly low and future health surveys with more participants are recommended. However, the precise cluster sampling used in this study resulted in a study population which is representative of the whole community in our region. Second, the measurements and clinical examination were performed by several physicians and nurses which has resulted in inevitable interobserver variation affecting the reliability of the clinical findings and measurements.

In conclusion, the prevalence rates of cardiovascular risk factors as well as metabolic syndrome are relatively high in our region. Moreover, IMT is affected by age, hypertension, DM, smoking, BMI, waist circumference and TG levels and is an appropriate predictor of atherosclerosis. Appropriate policies and actions should be undertaken to prevent the cardiovascular events in our regions.

Authors' Contributions

Kamran Bagheri Lankarani: Concept and design. Fariborz Ghaffarpasand: Design, analysis, and interpretation. Mojtaba Mahmoodi: Analysis, and manuscript preparation. Maryam Dehghankhalili: Interpretation, and manuscript preparation. Behnam Honarvar: Interpretation, and manuscript preparation. Mehrzad Lotfi: Design, and interpretation. Nima Zamiri: Concept and design. Sayed Taghi Heydari: Analysis, and Interpretation. Mohammad Kazem|Fallahzadeh: Design, and interpretation. Najmeh Maharlouei: Interpretation, and manuscript preparation. Mohammad Saeid Khaksar: Data gathering, and manuscript preparation. Bita Geramizadeh: Design, and interpretation.

Funding/Support

This research project was financially supported by health policy research center affiliated to Shiraz University of Medical Sciences.

References

1. Homer D, Ingall TJ, Baker HJ, O'Fallon WM, Kottke BA, Whisnant JP. Serum lipids and lipoproteins are less powerful predictors of extracranial carotid artery atherosclerosis than are cigarette smoking and hypertension. *Mayo Clin Proc.* 1991;**66**(3):259–67.
2. Willeit J, Kiechl S. Prevalence and risk factors of asymptomatic extracranial carotid artery atherosclerosis. A population-based study. *Arteriosclerosis, Thrombosis, and Vascular Biology.* 1993;**13**(5):661–8.
3. O'Leary DH, Polak JF, Kronmal RA, Kittner SJ, Bond MG, Wolfson SK, et al. Distribution and correlates of sonographically detected carotid artery disease in the Cardiovascular Health Study. The CHS Collaborative Research Group. *Stroke.* 1992;**23**(12):1752–60.
4. Bots ML, Hofman A, de Bruyn AM, De Jong PT, Grobbee DE. Isolated systolic hypertension and vessel wall thickness of the carotid artery. The Rotterdam Elderly Study. *Arteriosclerosis, thrombosis, and vascular biology.* 1993;**13**(1):64–9.
5. Crouse JR, Goldbourt U, Evans G, Pinsky J, Sharrett AR, Sorlie P, et al. Risk factors and segment-specific carotid arterial enlargement in the Atherosclerosis Risk in Communities (ARIC) cohort. *Stroke.* 1996;**27**(1):69–75.
6. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima-media thickness: a systematic review and meta-analysis. *Circulation.* 2007;**115**(4):459–67.
7. Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. Common carotid intima-media thickness and risk of stroke and myocardial infarction: the Rotterdam Study. *Circulation.* 1997;**96**(5):1432–7.
8. Lonn E. Carotid artery intima-media thickness--a new non-invasive gold standard for assessing the anatomic extent of atherosclerosis and cardiovascular risk? *Clin Invest Med.* 1999; **22**(4):158–60.
9. Bonithon-Kopp C. Prevalence of and risk factors for intima-media thickening: a literature review. *Intima-media thickness and atherosclerosis. Predicting the risk.* 1997:27–44.
10. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson J. K. . Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. *New England Journal of Medicine.* 1999;**340**(1):14–22.
11. Agewall S, Wikstrand J, Samuelsson O, Persson B, Andersson OK, Fagerberg B. The efficacy of multiple risk factor intervention in treated hypertensive men during long - term follow up. *Journal of internal medicine.* 1994;**236**(6):651–9.
12. Greenland P, Abrams J, Aurigemma GP, Bond MG, Clark LT, Criqui MH, et al. Prevention Conference V: Beyond secondary prevention: identifying the high-risk patient for primary prevention: noninvasive tests of atherosclerotic burden: Writing Group III. *Circulation.* 2000;**101**(1):E16–22.
13. American Diabetes A. Standards of medical care in diabetes--2011. *Diabetes Care.* 2011;**34 Suppl 1**:S11–61.
14. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension.* 2003;**42**(6):1206–52.
15. Salonen JT, Salonen R. Ultrasound B-mode imaging in observational studies of atherosclerotic progression. *Circulation.* 1993;**87**(3 Suppl):II56–65.
16. Burke GL, Evans GW, Riley WA, Sharrett AR, Howard G, Barnes RW, et al. Arterial wall thickness is associated with prevalent cardiovascular disease in middle-aged adults. The Atherosclerosis Risk in Communities (ARIC) Study. *Stroke.* 1995;**26**(3):386–91.
17. Kawagishi T, Nishizawa Y, Konishi T, Kawasaki K, Emoto M, Shoji T, et al. High-resolution B-mode ultrasonography in evaluation of atherosclerosis in uremia. *Kidney Int.* 1995;**48**(3):820–6.
18. Cuspidi C, Lonati L, Sampieri L, Leonetti G, Zanchetti A. Similarities and differences in structural and functional changes of left ventricle and carotid arteries in young borderline hypertensives and in athletes. *J Hypertens.* 1996;**14**(6):759–64.
19. Bots ML, van Swieten JC, Breteler MM, de Jong PT, van Gijn J, Hofman A, et al. Cerebral white matter lesions and atherosclerosis in the Rotterdam Study. *Lancet.* 1993;**341**(8855):1232–7.

20. Crouse JR, Craven TE, Hagaman AP, Bond MG. Association of coronary disease with segment-specific intimal-medial thickening of the extracranial carotid artery. *Circulation.* 1995;**92**(5):1141–7.
21. Davis PH, Dawson JD, Mahoney LT, Lauer RM. Increased Carotid Intimal-Medial Thickness and Coronary Calcification Are Related in Young and Middle-Aged Adults The Muscatine Study. *Circulation.* 1999;**100**(8):838–42.
22. Linhart A, Gariepy J, Giral P, Levenson J, Simon A. Carotid artery and left ventricular structural relationship in asymptomatic men at risk for cardiovascular disease. *Atherosclerosis.* 1996;**127**(1):103–12.
23. Mykkänen L, Zaccaro DJ, O'Leary DH, Howard G, Robbins DC, Haffner SM. Microalbuminuria and carotid artery intima-media thickness in nondiabetic and NIDDM subjects The Insulin Resistance Atherosclerosis Study (IRAS). *Stroke.* 1997;**28**(9):1710–6.
24. Aminbakhsh A, Mancini GB. Carotid intima-media thickness measurements: what defines an abnormality? A systematic review. *Clin Invest Med.* 1999;**22**(4):149–57.
25. Bots ML, Hofman A, Grobbee DE. Common carotid intima-media thickness and lower extremity arterial atherosclerosis. The Rotterdam Study. *Arteriosclerosis, Thrombosis, and Vascular Biology.* 1994;**14**(12):1885–91.
26. Simons PCG, Algra A, Bots ML, Banga JD, Grobbee DE, van der Graaf Y. Common carotid intima-media thickness in patients with peripheral arterial disease or abdominal aortic aneurysm: the SMART study. *Atherosclerosis.* 1999;**146**(2):243–8.
27. Schreiner PJ, Heiss G, Tyroler HA, Morrisett JD, Davis CE, Smith R. Race and gender differences in the association of Lp(a) with carotid artery wall thickness. The Atherosclerosis Risk in Communities (ARIC) Study. *Arterioscler Thromb Vasc Biol.* 1996;**16**(3):471–8.
28. Adams MR, Nakagomi A, Keech A, Robinson J, McCredie R, Bailey B, et al. Carotid intima-media thickness is only weakly correlated with the extent and severity of coronary artery disease. *Circulation.* 1995;**92**(8):2127–34.
29. Tahaghoghi S, Massarrat S. Iranian national health survey: a brief report. *Arch Iranian Med.* 2011;**12**(12):4.
30. Onat A. Metabolic syndrome: nature, therapeutic solutions and options. *Expert Opin Pharmacother.* 2011;**12**(12):1887–900.