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The 10-year Absolute Risk of Cardiovascular (CV) Events in Northern Iran: a Population Based Study

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ABSTRACT

Background: The present study was conducted to estimate 10-year cardiovascular disease events (CVD) risk using three instruments in northern Iran. **Material and methods:** Baseline data of 3201 participants 40-79 of a population based cohort which was conducted in Northern Iran were analyzed. Framingham risk score (FRS), World Health Organization (WHO) risk prediction charts and American college of cardiovascular / American heart association (ACC/AHA) tool were applied to assess 10-year CVD events risk. The agreement values between the risk assessment instruments were determined using the kappa statistics. **Results:** Our study estimated 53.5%of male population aged 40-79 had a 10 –year risk of CVD events≥10% based on ACC/AHA approach, 48.9% based on FRS and 11.8% based on WHO risk charts. A 10 –year risk≥10% was estimated among 20.1% of women using the ACC/AHA approach, 11.9%using FRS and 5.7%using WHO tool. ACC/AHA and Framingham tools had closest agreement in the estimation of 10-year risk≥10% (κ=0.7757) in meanwhile ACC/AHA and WHO approaches displayed highest agreement (κ=0.6123) in women. **Conclusion:** Different estimations of 10-year risk of CVD event were provided by ACC/AHA, FRS and WHO approaches.

Key words: 10-year cardiovascular risk, Framingham risk score, ACC/AHA tool, WHO risk prediction charts, Northern Iran.

1. INTRODUCTION

Cardiovascular disease (CVD) is the most important common cause of death in the worldwide. A larger part of the global burden of CVD is belong to low and middle income countries due to epidemiologic transition, from communicable to non-communicable diseases (1, 2).On the other hand, a downward trend of CVD mortality in developed countries could be resulted from therapeutic approaches and prevention procedures (3).To apply the global disease prevention strategies and implement the effective target segmented interventions it is required to recognize the populations at higher risk. On the other hand, to diagnose the populations at risk the cardiovascular risk assessment tools may be valuable for which several effective instruments were developed (4-6).Among several CVD risk assessment tools Framingham risk score is an old popular tool used widely in clinical practice and research studies (4). A newer instrument was proposed by the American college of cardiovascular and American heart association jointly tailored to the American population (5).Although no risk assessment tools were suggested specially to our country the WHO developed the risk prediction charts which one of them was suggested to use in our population (6).

Iran was considered a middle income country for which an increasing trend of non-communicable diseases is predicted (7, 8). As a result providing an estimate of cardiovascular events in the next years may be extremely valuable in its population. Therefore, this study was conducted to determine the 10-year cardiovascular risk among the population of northern Iran using three above mentioned risk assessment tools.

2. MATERIALS AND METHODS

Study participants

The data of a population based cohort study carried out in Amol, one of the most populous cities in northern Iran, in 2009-

2010 were used. A representative sample of Amol population was drawn out. Health centers in where each person of inhabitants had a health record were used to collect the relevant information. The sampling was described elsewhere (9).

Because we used the data of subjects aged 40 to 79 years, the data of 3201 participants of 6140 subjects of cohort study were included to analyze. A schematic diagram of participants was displayed in Figure 1.

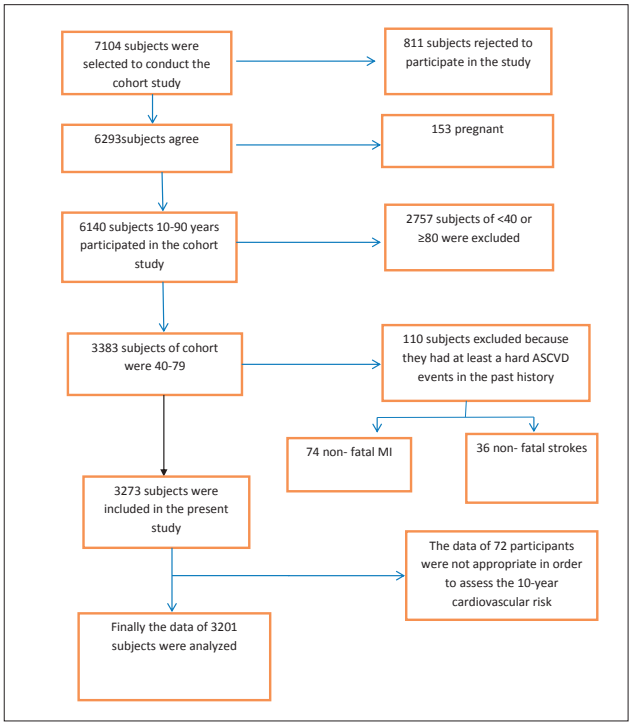

Figure 1.A schematic diagram of our participants

Data collection

Trained healthcare workers collected related data including medical and personal history, anthropometric data and also blood pressure. For laboratory measures a venous blood sample was drawn from each participant following 10-hour fasting to assess fasting blood sugar (FBS) and lipid profiles.

FBS, triglycerides (TGs) and High-density lipoprotein (HDL) were assessed using the BS200 Auto analyzer (Mindray, China) measured by the glucose oxidase/peroxidase-4 aminophenazone-phenol method and TGs were measured using glycerol-3-phosphate oxidase peroxidase aminophenazone (Trulab N, Trulab Pars Azmoon, Iran). HDL values were assessed after dextran sulfate-magnesium chloride precipitation of the non–HDL cholesterol samples. Ten percent of the blood samples were re-checked by the Iranian National Reference Laboratory with the coefficients of variation being between 1.7% and 3.8% of all laboratory values.

Statistical analysis

To estimate the 10-year CVD events, the risks were calculated separately for men and women based on ACC/AHA equations, Framingham risk scores and WHO / ISH risk prediction charts. In ACC/AHA approach, the race- and sex-specific multivariate equations were used to compute the 10-year risk for a first hard atherosclerotic cardiovascular disease (ASCVD) event, including coronary heart disease death, nonfatal myocardial infarction, and fatal or nonfatal stroke, in non-Hispanic African Americans and non-Hispanic American whites aged 40 to 79 years. We used the sex-specific non-Hispanic American white version of pooled cohort multivariate equations to compute 10-year risk for a first hard ASCVD event. In these equations, the variables of age, current smoker (yes/no), total blood cholesterol; HDL, systolic blood pressure values and the treatment status of blood pressure (yes/no) were used. The risks were also estimated according to Framingham approach. In this approach the sum of the Framingham point scores corresponding to the categories of age, systolic blood pressure (treated or untreated), HDL, total cholesterol (by the age group) and smoking status (by the age group)was separately computed by gender. Thus the related risks corresponding to the sum of Framingham point scores were obtained for each participant. We obtained the relevant 10- year cardiovascular risks using WHO risk prediction charts too. These charts estimate the risks in five categories, <10%, 10 to <20%, 20% to <30%, 30% to <40% and ≥40%. There are two versions of WHO risk chart based on the use of the cholesterol for all epidemiological sub-regions of WHO member states. We used the Eastern Mediterranean region B (EMR B:low child mortality and low adult mortality) version of risk prediction charts included cholesterol to estimate the risk in addition to age, sex, smoking status SBP and diabetes status.

In order to estimate the prevalence of a 10-year cardiovascular risk ≥10% and ≥20%, the calculated risks were converted to a dichotomous scale based on thresholds of 10% and 20%. As a result the continuous risks computed by ACC/AHA, the discrete risks estimated by the FRS and categorical risks obtained

Characteristics	Mean ± SD in men (n=1826)	Mean ± SD in women (n=1375)	*p*-value *
Age (year)	55.11±10.40	54.04 ± 9.65	0.0030
WC (cm)	93.47 ± 11.19	96.17 ± 11.54	<0.0001
BMI ()	27.14 ± 4.25	31.16 ± 5.05	<0.0001
	68.5 (66.4-70-6) £	88.9 (87.3-90.5) £	<0.0001
Current smoker§	30.3 (28.0-32.6)	0.6 (0.12-1.0)	<0.0001
DBP (mm Hg)	77.92 ± 13.07	79.31 ± 13.11	0.0031
	31.25 (29.1-33.4) £	35.4 (32.9-37.9) £	0.0131
SBP (mm Hg)	119.26 ± 17.13	121.35 ± 18.54	0.0010
	24.5 (22.5- 26.4) £	30.5 (28.1 -33.0) £	0.0001
FBS (mg/dl)	103.22 ± 35.56	113.40 ± 49.08	<0.0001
	33.4 (31.3- 35.6) £	44.4 (41.8- 47.1) £	<0.0001
TG (mg/dl)	149.80 ± 87.89	155.08± 90.86	0.1029
	37.4 (35.1 39.7) £	41.4 (38.7-44.0) £	0.0249
Total cholesterol (mg/dl)	187.21 ± 41.25	200.19 ± 42.84	<0.0001
	37.2 (35.0-39.4) £	50.0 (47.4-52.7) £	<0.0001
LDL (mg/dl)	110.89 ± 30.76	117.70 ± 31.28	<0.0001
	25.4(23.4 -27.4) £	33.1(30.6-35.6) £	<0.0001
HDL (mg/dl)	42.96 ± 11.65	44.61 ± 12.00	0.0001
	45.6(43.3- 47.9) £	68.4 (65.9- 70.8) £	<0.0001

*Table 1. Baseline demographic, anthropometric and metabolic characteristics of study participants between 40–79 years of age. AVI indicates abdominal volume index; BMI, body mass index; DBP, diastolic blood pressure; FBS fasting blood sugar; HC, hip circumference; HDL,high-density lipoprotein; LDL,low-density lipoprotein; SBP, systolic blood pressure; SD, standard deviation; TG, triglyceride; WC indicates waist circumference; WHR, waist to hip ratio; WHtR, waist to height ratio. * Significance level for difference between men and women was considered at p<0.05. § Prevalence and related confidence interval of smoking, £ prevalence and related confidence interval ofBMI≥25 (),DBP≥85mmHg, FBS≥100mg/dl,HDL≤40 in men and HDL≤50 in women, LDL≥130mg/dl, SBP ≥130mmHg, TG≥150mg/dl, Total cholestrol≥200mg/dl.*

Age	40-79			40-59			60-79		
Sex	Male	Female	P-value	Male	Female	P-value	Male	Female	P-value
Approaches	10-year CVD events ≥10%								
ACC/AHA	53.5(51.2- 55.7)	20.1 (18.0- 22.2)	<0.0001	31.8 (29.1 -34.4)	3.5 (2.4 -4.7)	<0.0001	97.4 (96.1 -98.6)	59.5 (54.7-64.2)	<0.0001
Framingham	48.9 (46.6 -51.2)	5.7 (4.5 -6.9)	<0.0001	29.5 (27.0 -32.1)	1.1 (0.47 -1.8)	<0.0001	88.1 (85.5 -90.7)	16.5 (12.9 -20.1)	<0.0001
WHO	11.8 (10.4-13.3)	11.9 (10.3- 13.6)	0.9310	0.78 (0.30 -1.3)	1.8 (0.95 -2.6)	0.0690	34.5 (30.7-38.2)	36.5 (31.9-41.0)	0.5046
10-year CVD events ≥20%									
ACC/AHA	28.1 (26.0- 30.2)	6.8 (5.4 -8.1)	<0.0001	7.7 (6.2 -9.2)	0.41 (0.0- 0.82)	<0.0001	69.4 (65.7- 73.1)	21.9 (17.9-25.9)	<0.0001
Framingham	14.4 (12.8 -16.0)	1.0 (0.49 .1.6)	0.0001	7.0 (5.5-8.4)	0	<0.0001	29.4 (25.7-33.0)	3.4 (1.7 -5.2)	<0.0001
WHO	3.1 (2.4- 3.9)	4.0 (3.0 -5.0)	0.1914	0.31 (0.0-0.62)	0.49 (0.06 -0.91)	0.5055	8.9(6.7-11.2)	12.4 (9.3- 15.5)	0.0705

Table 2. The prevalence of a 10-year cardiovascular events≥10% and≥20% among present study sub-populations using three risk assessment tools including ACC/AHA instrument, FRS and WHO risk prediction chart. ACC/AHA indicates American College of Cardiology /American Heart Association; WHO, world health organization; CVD cardiovascular disease

from WHO risk charts were changed into binary scales of risk. The prevalence of 10-year risk ≥10% and ≥20% were calculated in the total population by gender and by the selected age groups, 40-59 and 60-79 years. The agreement values between risk assessment tools were computed using the κ statistics.

The significant level was considered 0.05 and all statistical analyses were performed using the STATA software, version 12 (Stata Corp, Texas, USA).

3. RESULTS

Table 1 shows the baseline characteristics of our participants. Anthropometric characteristics including WC and BMI, DBP and SBP and also laboratory values were significantly higher among women. While the prevalence of smoking was considerably higher in men (30.3% versus 0.6%), women had a significantly higher prevalence of a low HDL level (p-value<0.001).

We divided the population into four groups including male age group of 40-59, male of 60-79, female of 40-59 and female of 60-79. The data on male and female of 40-79 were also analyzed in addition to four above mentioned age groups separately .A significantly larger part of our population will have a 10 -year risk ≥10% and 20%based on estimations of ACC/AHA instrument in comparison with estimations of WHO risk charts, of course, except for 10-year risk≥ 20% in women of age group of 40-59 (p-value=0.8085). On the other hand ACC/AHA approach gave us a significantly greater estimate of 10-year risk of CVD among our population comparison with FRS for age groups of 40-79 and 60-79, both for male and female. In age group of 40-59, ACC/AHA instrument provided only a significantly greater estimate of risk≥10% (p-value=0.0005) in women, while other comparisons in this age group were not significant. On the other hand in the comparison of FRS and WHO approaches a significantly greater proportion of the population was estimated to have a 10-year risk of cardiovascular events ≥10% and ≥ 20% by FRS in age groups of 40-80 and 60-80, both in male and female (all p-values were <0.0001). In the age group of 40-59, except for 10-year risk ≥10% in women (p-value=0.2525), FRS significantly made a greater estimate of the population will be at risk of CVD (both 10-risk≥10% and ≥20%).

Table 2 lists an estimate of the population at 10-risk in which a significantly higher estimation was provided for men compared to women using both ACC/AHA and FRS risk assessment tools (all p-values were <0.0001), while no significant difference was detected by the use of WHO risk prediction charts between the two sexes.

Table 3 shows the results of the kappa coefficients between three cardiovascular risk assessment tools in the prediction of CVD events in which the results of the upper half of the table are related to women. In age group of 40-79 the ACC/AHA and Framingham tools showed the highest agreement values to estimate the 10-year risk in meanwhile in women ACC/AHA and WHO tools had the highest values. More details were reported in Table 3.

Risk assessment tools	10-year risk≥ 10%			10-year risk≥ 20%		
	ACC/AHA	Framingham	WHO	ACC/AHA	Framingham	WHO
40-80						
ACC/AHA	1	0.3740 ±0.0213*	0.6123± 0.0258	1	0.2484± 0.0178	0.4901± 0.0261
Framingham	0.7757± 0.0233£	1	0.4976± 0.0248	0.4864± 0.0215	1	0.2940± 0.0211
WHO	0.2053± 0.0142	0.2306± 0.0153	1	0.1549± 0.0125	0.2748± 0.0173	1
40-60						
ACC/AHA	1	0.3895± 0.0275	0.4481± 0.0305	1	0.0000 ± 0.0000	-0.0046± 0.0319
Framingham	0.7287± 0.0286	1	0.5453± 0.0312	0.5118± 0.0286	1	0.0000± 0.0000
WHO	0.0279± 0.0067	0.0255± 0.0071	1	0.0758± 0.0109	0.0842± 0.0115	1
60-80						
ACC/AHA	1	0.2369± 0.0320	0.4476± 0.0447	1	0.2258± 0.0314	0.4614 ± 0.0472
FRS	0.2397± 0.0304	1	0.3974± 0.0431	0.3107± 0.0295	1	0.2897 ± 0.0391
WHO	0.0274± 0.0095	0.1084± 0.0201	1	0.0831± 0.0162	0.3026± 0.0320	1

*Table 3. The agreement value between risk assessment tools in various subpopulations of study. *The results of the upper half of the table are related to women; £ kappa± standard error; ACC/AHA indicates American College of Cardiology /American Heart Association, WHO world health organization*

4. DISCUSSION

Different estimates of 10- year cardiovascular risk were computed by the use of three risk assessment tools. While ACC/AHA gave us a significantly greater estimate of risk, FRS and particularly WHO display a conservative image of 10-years risk of CVD events. The present study estimated a larger part of the male population is at risk of cardiovascular disease in the next decade in comparison with the female population. The prevalence of 10-years cardiovascular risk≥10% and ≥20% was increased considerably in age group of 60-79 compared to age group of 40-59, so that a dramatically increase was estimated by all three risk assessment tools among former. We also examined the agreement values between three risk assessment instruments mutually of which the higher values were calculated for ACC/AHA and FRS approaches in men and also for ACC/AHA and WHO approaches in women.

A significant proportion of our population, particularly men were at risk for 10-year CVD events, although among three risk assessment tools a lower estimation was obtained using the WHO tool. A higher risk of CVD events in the incoming years is predictable for our country, because Iran is considered a middle income country in which an increasing trend of non-communicable disease will be foreseeable due to experiencing the epidemiologic transition (7, 8).Urbanization and industrialization imposed a sedentary lifestyle in addition to shift from a Mediterranean diet to western diet (10, 11).

Northern Iran is a wealthier region in the country where although benefited from an acceptable access to health care facilities, it was suffering from a high fat diet, sedentary lifestyle and their outcomes particularly obesity (12, 13). It is evident the obesity is strongly associated with cardiovascular risk factors, including, high blood pressure, insulin resistance, dyslipidemia (14-17). Although the obesity measures were not directly used in any of the risk assessment tools, the CVD risk factors which are related to obesity were entered into the instruments to provide an estimate of the CVD events. On the other hand, with regard to high prevalence of obesity in our population, the higher cardiovascular events will be forecasted in coming years in an agreement with ACC/AHA estimations.

A higher estimate of 10-year risk for male population was expected, because most of the risk assessment tools were developed based on sex in which a higher susceptibility to CVD for men is default. However,no difference of risk was significantly estimated between two sexes by WHO risk charts. On the other hand, most of the cardiovascular risk factors were significantly higher in women except for smoking and HDL so that former was almost exclusively to men.

None of the risk assessment tools were able to image expected picture of population at risk. While ACC/AHA and FRS provided support for a lower risk of CVD among female compared to male in age group of 40-60, no significant difference was detected applying the WHO tool. It is seemed WHO tool estimated falsely low the 10-year CVD risk among men of age group of 40-60. On the other hand FRS was not able to represent a correct status of CVD risk in age group of 60-80 in such a way that an expected dramatic increasing risk in women after menopause period was not portrayed appropriately. The results of FRS were not in agreement with loss of estrogen protection against to CVD events after menopause. Although the ACC/AHA tool well described the increasing trend of risk in both two sexes with the increase of age, it was not success to characterize risk in age group of 60-79 of female with regard to a higher risk of cardiovascular events expected in this age group of women.

While a higher agreement between ACC/AHA approach and FRS was revealed in men, the agreement was higher between ACC/AHA and WHO risk charts in women. It is seemed a male predominance susceptibility to CVD is less default in WHO approach. As a result the estimations of WHO will be more agreement with estimations of ACC/AHA approach in women.

WHO risk charts are applied visually with an easier approach than two other risk tools in which HDL was not included. WHO and FRS obtain categorized and discrete estimation of risks bounded to ≥0.3 and ≥0.4 respectively, while ACC/AHA calculates continuous risks no bounded to any specific value. This property enables it to produce the continuous 10-year cardiovascular risk from 0 to 1 flexibly. However, despite the mentioned potential theoretical advantages, ACC/AHA approach was not tailored to non –American population. As a result, to validate it in prospective large sample size studies, the results produced by it should be cautiously translated into clinical practice or community based CVD risk management policies.

Our study estimated the 10-year risk of CVD by the use of three powerful approaches and obtained the agreement values between them in a population based study. However, we were not able to determine the validity of the instruments due to cross sectional design of the study.

5. CONCLUSION

Although very different estimations of 10-year risk of CVD events were provided by ACC/AHA, FRS and WHO approaches, ACC/AHA approach showed a higher agreement with FRS and WHO tools in men and women of age group of 40-79 respectively.

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CONFLICT OF INTEREST: NONE DECLARED.

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