Original Article

Journal of Occupational Health and Epidemiology

Journal Homepage: https://johe.rums.ac.ir/

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Rafsanjan University of Medical Sciences

Ten-Year Cardiovascular Disease Risk Evaluation in PERSIAN Guilan Cohort Study: A Cross-Sectional Study

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Citation: Hasandokht T, Maroufizadeh S, Joukar F, Salari A, Mansour-Ghanaei F. Ten-Year Cardiovascular Disease Risk Evaluation in PERSIAN Guilan Cohort Study: A Cross-Sectional Study. J Occup Health Epidemiol. 2023;12(2):78-85.

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Article history
Received: Oct 2022
Accepted: Apr 2023

10. 61186/johe.12.2.78

Print ISSN: 2251-8096
Online ISSN: 2252-0902

Peer review under responsibility of Journal of Occupational Health and Epidemiology

Abstract

Background: Cardiovascular disease (CVD) is one of the most prevalent diseases worldwide including in the Asian population. CVD risk assessment provides support for policymakers for prevention strategies. This research aimed to estimate the 10-year CVD risk and evaluate the agreement between three risk scores.

Materials and Methods: A descriptive study was conducted based on 9398 subjects aged 40–70 years from 10520 PERSIAN Guilan Cohort Study (PGCS) participants in Guilan, Iran. Baseline demographic data, comorbidities, and CVD variables were derived from cohort records. The 10-year CVD risk events for every individual were calculated using three risk score models including the American College of Cardiovascular / American Heart Association (ACC/AHA) tool, Framingham Risk Score (FRS), and World Health Organization (WHO) chart. The agreement between the CVD risk scores was evaluated using the kappa statistics.

Result: The proportion of high-risk people based on WHO, FRS, and ACC/AHA was 17.5%, 16.1%, and 5.4%, respectively. WHO risk score can find the highest frequency of females with high CVD risk scores. The best agreement was observed between FRS and ACC/AHA (κw=0.672, complete agreement=82.3%). Agreement between the WHO and ACC/AHA as well as WHO and FRS was reported as κw=0.351 and κw=0.357, respectively.

Conclusions: WHO risk chart found the greatest number of people as the high-risk category. A substantial agreement was observed between FRS and ACC/AHA.

Keywords: Cardiovascular Diseases, Risk Assessment, Cohort Study, Framingham Heart Study

Introduction

Cardiovascular diseases (CVDs) are the most important public health problem in the world [1], particularly in low- and middle-income countries [2]. The proportions of mortality related to ischemic heart disease (IHD) from all death among Iranian men and women were 40% and 44%, respectively [3]. Several health behaviors and factors such as

unhealthy diet, obesity, physical inactivity, smoking, high blood pressure, glucose intolerance, and high cholesterol level contribute to predisposition to CVD. A national report of STEPwise approach to surveillance (STEPS) study indicated less than 4 % of Iranian adults have ≥ 6 ideal controlled CVD risk factors in 2016 [4]. Hence, this issue needs immediate multicomponent prevention programs at the public health and individual levels. A recent study showed the high healthcare cost for secondary prevention in high-risk CVD people in first year, while it substantially decreased over time [5]. To reduce CVD healthcare cost and effectively implement prevention programs at the community level, target oriented strategies have been proposed in previous studies [6]. For this purpose cardiovascular risk prediction models are known as a practical method to identifying those at higher risk who will derive the greatest benefit [7]. Several CVD risk score models have been presented including Framingham risk score (FRS), Systematic Coronary Risk Evaluation (SCORE) algorithm, world health organization (WHO/ISH) risk chart, and American College of Cardiology/American Heart Association (ACC/AHA) risk score [8]. WHO recommended a prevention program for non-communicable disease (NCD) as well as a CVD risk chart for stratification of CVD risk in the low- and middle-income countries. In response to substantial CVD burden in Iran, WHO CVD risk chart was used in the national prevention program. We estimate the frequency of 10-year CVD risk among Iranian people based on PERSIAN Guilan Cohort Study using ACC/AHA, Framingham risk score, and WHO risk chart as well as assess the agreement between the three risk scores.

Materials and Methods

This is a descriptive study on PERSIAN Guilan Cohort Study (PGCS) (The Ethics Approval No was IR.GUMS.REC.1398.480); a prospective, population-based cohort study was designed in Guilan province as described in detail previously [9-11]. In brief, The Guilan cohort study (GCS) involved 10520 participants aged within 35-70 years in northern Iran, Guilan province, between October 8, 2014 and January 20, 2017 as part of the Prospective Epidemiological Research Studies in Iran (PERSIAN). Eligible subjects were invited to participate in the study through telephone call. All study data including demographic characteristics, socio-economic status, lifestyle and sleep habits, anthropometric indices, blood pressure, and biological samples were recorded based on the cohort protocol. Also, annual active follow-ups were planned for next 15 years for all participants.

We excluded data related to those with a history of CVD. According to GCS, all data related to those with a past history of myocardial infarction, coronary angioplasty, coronary bypass surgery, stroke, and any history of ischemic heart disease based on self-report and patient's health data were excluded.

For the present study, the data related to individuals aged 40-70 years were used. The data included:

1) Demographic factors (age, sex, place of residence (city or rural), marital status (single, married, widow, divorced), occupation (employed, unemployed), years of education),

2) Anthropometric indices (weight, height, body mass index: BMI),

3) History of smoking and alcohol,

4) Clinical data (hypertension (HTN), diabetes mellitus (DM), taking anti-hypertensive medications,

5) Laboratory data such as fasting blood sugar (FBS), triglycerides (TG), high-density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol (TC), and systolic blood pressure (SBP). Body mass Index (BMI) was classified as underweight (BMI<18.5 kg/m2), normal weight (BMI= 18.5-24.99 kg/m2), overweight (BMI= 25-29.9 kg/m2), and obese (BMI≥ 30 kg/m2).

The 10-year CVD events for every individual were calculated based on the three risk scores models (ACC/AHA, FRS, WHO/ISH).

Cardiovascular Disease Risk Assessment Tools

ACC/AHA: The American College of Cardiology/ American Heart Association Atherosclerotic Cardiovascular Disease (ACC/AHA ASCVD) Risk Score estimates the 10-year risk for atherosclerotic CVD, defined as fatal or nonfatal myocardial infarction, or fatal or non-fatal stroke, based on the pooled cohort equations. The variables included age, gender, race (other), total cholesterol, HDL, systolic blood pressure, on treatment for hypertension, smoking status, and diabetes [12]. We defined three categories as low risk (calculated risk score <5%), moderate (risk = 5% -20%), and high (risk ≥ 20 %). ASCVD risk was calculated at individual level for each participant using COX proportional hazard model based on the coefficients of ACC/AHA model [13].

FRS: Framingham Risk Score is based on the data derived from middle-class White Americans in the 1970s to 1980s. It estimates the 10-year risk of CVD (coronary artery disease, stroke, peripheral vascular disease, congestive heart failure, and cardiac death) using age, gender, systolic blood pressure, total cholesterol, HDL, smoking status,

treatment of hypertension, and diabetes status [14]. We used the Framingham multivariable risk Function which has been formulated by D'Agostino et al [15]. FRS was defined as low (risk <10%), moderate (risk = 10%-20%), and high (risk ≥ 20%).
WHO/ISH: The WHO prediction paper charts for each sub-region were developed to estimate the 10-year risk of CVD (myocardial infarction, angina pectoris, and stroke) based on several variables including age, gender, diabetes status, smoking status, systolic blood pressure, and total cholesterol [14]. We calculated the risk for each individual using a R syntax code based on Collins & et al study [16]. WHO risk score was classified as low (risk <10%), moderate (risk = 10 % - 20 %), and high (risk ≥ 20%).
In the present study, continuous variables were expressed as mean ± standard deviation (SD) while categorical variables as number (percentage). Demographic and clinical characteristics between males and females were compared using independent t test for continuous variables, and chi-square test for categorical variables. The weighted kappa coefficient (κw) was used to assess agreement between the three CVD risk assessment tools. The value of κw ranges from -1 to 1. A κ_w value of 0 indicates there is no agreement, whereas a κw value of 1 indicates perfect agreement. Values of κw are often interpreted as follows: <0.20, poor; 0.21-0.40, fair; 0.41- 0.60, moderate; 0.61-0.80, substantial; >0.80, very good. All data analyses were performed using SPSS for windows, version 16.0 (SPSS Inc., Chicago, IL, USA), except for the κw values, which were calculated using MedCalc for Windows, version 18.9.1 (MedCalc Software, Ostend, Belgium).

Results

After excluding the data related to those with a history of CVD (10.6%), 9398 individuals aged 40-70 were entered in the study (Figure 1). The demographic and clinical characteristics of the participants are outlined in Table 1. The mean age of the participants was 52.53 ± 8.25 years ranging within 40-73 years. Of the participants, 53.9% were female and more than 24% were smoker. The frequency of DM, HTN, and overweight/obese was 24.4%, 43.7%, and 72.5%, respectively.

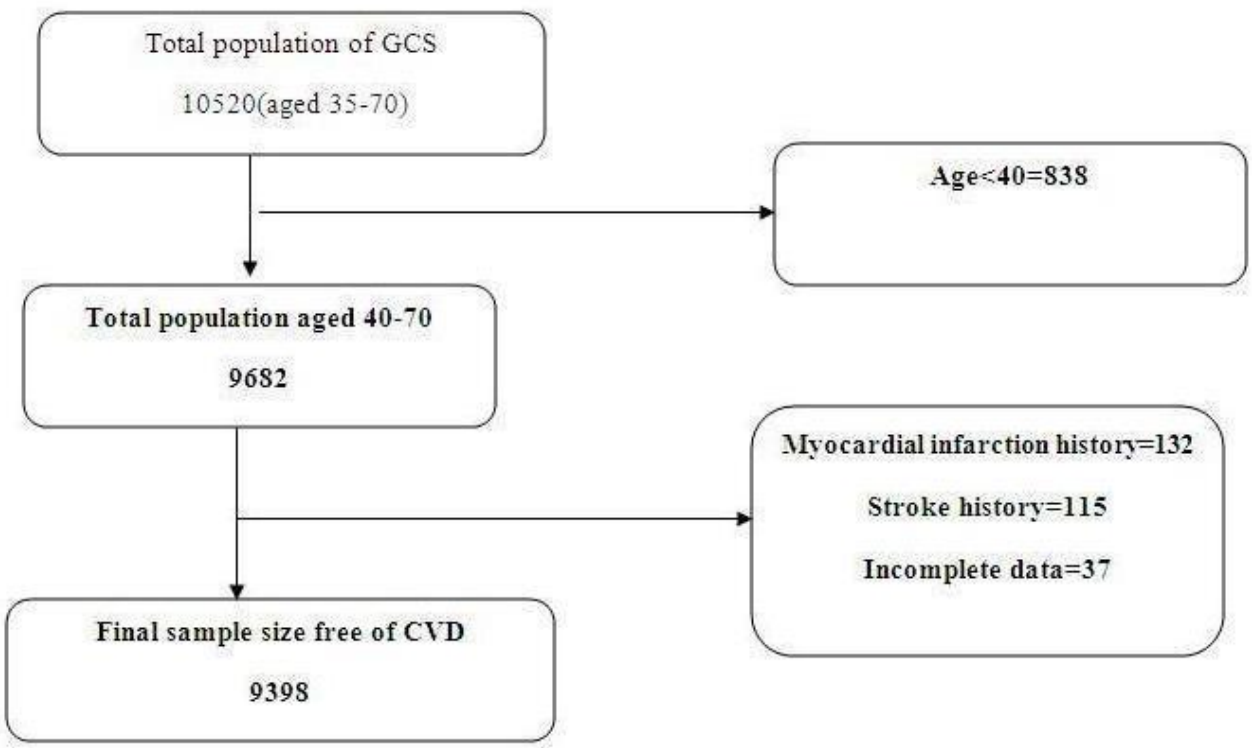

Fig. 1. Flowchart of the study population
GCS= Guilan cohort study, CVD= cardiovascular disease

Table 1. Demographic and clinical characteristics of the participants in the PERSIAN Guilan Cohort Study by sex

		Total (n=9398)	Male (n=4337)	Female (n=5061)
Age (years), mean ± SD		52.53 ± 8.25	52.49 ± 8.21	52.57 ± 8.29
Marital status, n (%)	**Single**	263 (2.8)	60 (1.4)	203 (4.0)
	Married	8519 (90.6)	4210 (97)	4309 (85.1)
	Widowed	512 (5.4)	43 (1.0)	469 (9.3)
	Divorced/Separated	104 (1.1)	24 (0.6)	80 (1.6)
Place of residence, n (%)	**Urban**	4172 (44.4)	1855 (42.8)	2317 (45.8)
	Rural	5226 (55.6)	2482 (57.2)	2744 (54.2)
	Years of education (years)	6.49 ± 4.49	7.56 ± 4.49	5.57 ± 4.28
Occupation, n (%)	**Employed**	5134 (54.6)	3848 (88.7)	1286 (25.4)
	Unemployed	4264 (45.4)	489 (11.3)	3775 (74.6)
	BMI (kg/m^2), mean ± SD	28.13 ± 5.10	26.01 ± 4.19	29.95 ± 5.10
BMI, n (%)	**Underweight**	124 (1.3)	97 (2.2)	27 (0.5)
	Normal	2463 (26.2)	1704 (39.3)	759 (15.0)
	Overweight	3750 (39.9)	1858 (42.8)	1892 (37.4)
	Obese	3061 (32.6)	678 (15.6)	2383 (47.1)
Smoking, n (%)	**Yes**	2305 (24.5)	2253 (51.9)	52 (1.0)
	No	7093 (75.5)	2084 (48.1)	5009 (99.0)
Alcohol, n (%)	**Yes**	1243 (13.2)	995 (22.9)	248 (4.9)
	No	8155 (86.8)	3342 (77.1)	4813 (95.1)
Diabetes, n (%)	**Yes**	2291 (24.4)	884 (20.4)	1407 (27.8)
	No	7107 (75.6)	3453 (79.6)	3654 (72.2)
Hypertension, n (%)	**Yes**	4104 (43.7)	1684 (38.8)	2641 (52.2)
	No	5294 (56.3)	2653 (61.2)	2420 (47.8)
Antihypertensive drug use, n (%)	**Yes**	2025 (21.5)	834 (19.2)	1191 (23.5)
	No	7373 (78.5)	3503 (80.8)	3870 (76.5)
SBP (mm Hg), mean ± SD		118.57 ± 16.74	119.07 ± 16.56	118.14 ± 16.88
LDL (mg/L, mean ± SD		113.35 ± 32.04	112.63 ± 31.65	113.96 ± 32.35
HDL-c (mg/dL), mean ± SD		48.58 ± 11.04	46.64 ± 10.53	50.25 ± 11.20
TC (mg/dL), mean ± SD		193.57 ± 38.29	191.79 ± 38.16	195.10 ± 38.34
TG (mg/dL), mean ± SD		160.6 ± 101.8	165.7 ± 111.7	156.29 ± 92.40
FBS (mg/dl), mean ± SD		105.07 ± 37.71	103.85 ± 35.42	106.12 ± 39.54

SD: Standard Deviation; BMI: Body Mass Index; SBP: Systolic Blood Pressure; LDL, Low Density Lipoprotein; HDL: High Density Lipoprotein; TC: Total Cholesterol; TG, Triglyceride; FBS: Fasting Blood Sugar.

Table 2 presents the distribution of CVD risk scores based on ACC/AHA, FRS, and WHO/ISH severity cutoffs. The frequency of people with high CVD risk according to ACC/AHA, FRS, and WHO/ISH was 5.4%, high, 16.1%, 17.5%, respectively. The frequency of high CVD risk score in males was higher than in females based on all three risk scores.

Table 2. Distribution of estimated 10-year risk of CVD events using three cardiovascular disease risk assessment tools in the PERSIAN Guilan Cohort Study by sex and age group

CVD Risk Score		Total	Age		p-value	Sex		p-value
			<55 years	≥55 years		Male	Female	
ACC/AHA	**Low (<5%)**	5752 (61.2)	4650 (81.6)	1102 (29.8)	<0.001	1736 (40.0)	4016 (79.4)	<0.001
	Moderate (5 % to 20%)	3136 (33.4)	1006 (17.7)	2130 (57.6)		2143 (49.4)	993 (19.6)	
	High (≥20%)	510 (5.4)	43 (0.8)	467 (12.6)		458 (10.6)	52 (1.0)	
FRS	**Low (<10%)**	5750 (61.2)	4440 (77.9)	1310 (35.4)	<0.001	1724 (39.8)	4026 (79.5)	<0.001
	Moderate (10% to 20%)	2137 (22.7)	1000 (17.5)	1137 (30.7)		1328 (30.6)	809 (16.0)	
	High (≥20%)	1511 (16.1)	259 (4.5)	1252 (33.8)		1285 (29.6)	226 (4.5)	
WHO/ISH	**Low (<10%)**	6588 (70.1)	5352 (93.9)	1236 (33.4)	<0.001	2996 (69.1)	3592 (71.0)	<0.001
	Moderate (10% to 20%)	1167 (12.4)	251 (4.4)	916 (24.8)		483 (11.1)	684 (13.5)	
	High (≥20%)	1643 (17.5)	96 (1.7)	1547 (41.8)		858 (19.8)	785 (15.5)	

ACC/AHA: American College of Cardiology/American Heart Association; FRS: Framingham Risk Score; WHO/ISH: World Health Organization/International Society of Hypertension

Fig. 2 indicates that 23.5% of the study population were in the high-risk group according to at least one high CVD risk score; 11.0% were classified as high CVD risk score based on at least two scores, and 4.55% were as high CVD risk base on all three. None of the study population had a high CVD risk score based on only ACC/AHA. However, 5.15% of people were in the high-risk group only by FRS and 7.32% of our study subjects were classified as high risk only by WHO/ISH (Fig. 2).

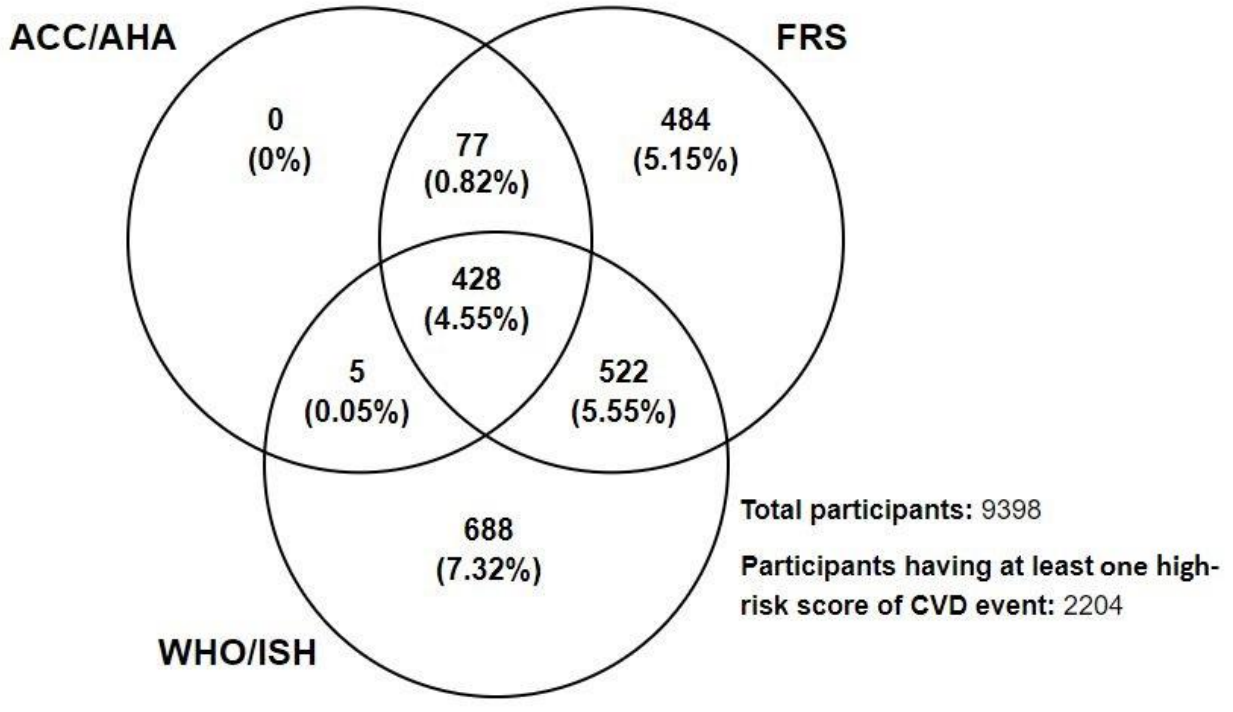

Fig. 2. Distribution of high estimated 10-year risk of CVD events (≥20%) using three cardiovascular disease risk assessment tools in the PERSIAN Guilan Cohort Study.

Note. ACC/AHA: American College of Cardiology/American Heart Association; FRS: Framingham Risk Score; WHO/ISH: World Health Organization/International Society of Hypertension

Regarding CVD severity risk score, a complete agreement was obtained between the three CVD risk assessment tools (i.e., all CVD risk assessment tools ... with each other) for 5647 (60.1%) participants. As reported in Table 3, the highest agreement was found between ACC/AHA and FRS tools (κw=0.672, complete agreement=82.3%), which is considered substantial. The agreements between ACC/AHA and WHO/ISH tools as well as between FRS and WHO/ISH tools were fair (κw=0.351 and κw=0.357, respectively).

Table 3. Agreement between CVD risk assessment tools in the PERSIAN Guilan Cohort Study

		ACC/AHA			**Weighted kappa coefficient**	**Complete agreement, n (%)**
		Low	**Moderate**	**High**		
FRS	**Low**	5424	326	0	0.672	7733 (82.3%)
	Moderate	328	1804	5		
	High	0	1006	505		
		ACC/AHA			Weighted kappa coefficient	Complete agreement, n (%)
		Low	Moderate	High		
WHO/ISH	**Low**	5174	1406	8	0.351	6228 (66.3%)
	Moderate	477	621	69		
	High	101	1109	433		
		FRS			Weighted kappa coefficient	Complete agreement, n (%)
		Low	Moderate	High		
WHO/ISH	**Low**	5002	579	169	0.357	6285 (66.9%)
	Moderate	1280	333	524		
	High	306	255	950		

ACC/AHA: American College of Cardiology/American Heart Association; FRS: Framingham Risk Score; WHO/ISH: World Health Organization/International Society of Hypertension

Discussion

This paper reports the distribution of 10-year CVD risk events in a rural and urban population based on a cohort study in north of Iran according to ACC/AHA, FRS, and WHO/ISH tools. Also, we assessed the agreement of these risk assessment tools. According to our results, a large proportion of the study participants without known CVD had CVD risk factors such as DM, HTN, and smoking, which was consistent with the findings reported in national studies [3, 4]. According to a study on non-communicable diseases' risk factors in Iran, HTN, DM, and smoking were responsible for a considerable number of deaths in 2019 [17]. Dramatically, a modeling study projected about 9.2 million of Iranian people would have DM by 2030 [18].

Our findings revealed a remarkable number of individuals with high and moderate 10-year CVD risk based on all three CVD risk assessment tools.

The most frequency of high CVD risk was reported based on WHO/ISH tool followed by FRS and ACC/AHA. WHO risk score found 17.5% of the study population as high risk which was near the result obtained from FRS (16%). However, only 5% of population was high risk base on AHA risk score. Furthermore, we observed WHO risk chart can find most individuals as high CVD risk among those older than 50 years old. However, most people with high 10-year CVD risk in younger was reported by FRS. In parallel with our finding, Ofori et al. reported 15.2% and 16.9% were classified as high CVD risk according to WHO risk score and FRS, respectively [19]. Another study on diabetic patients reported that the frequency of individuals with high 10-year CVD risk using FRS and AHA was 16.31% and 12.39%, respectively [20]. However, more than 26% of a study population of the central part of Iran were classified as high CVD risk based on FRS but only 4.2% of those were high risk based on the WHO chart [21]. Dramatically, our findings indicated more than 23% of study population were at high CVD risk based on at least one risk score.

Hence, implementing prevention strategies seems to be important. The present study reported all people who were deemed as high CVD risk by AHA were classified as high-risk group according to the two other risk scores. Nevertheless, we have a number of people who were classified as high risk only by WHO or FRS. A considerable agreement was reported between ACC/AHA and FRS, while a slight concordance was seen between ACC/AHA and WHO/ISH risk scores as well as between FRS and WHO/ISH. Parallel with the present study regarding low agreement between WHO chart and other two risk score, a recent study conducted in Iran reported poor agreement between the result of WHO chart and FRS (kappa 0.17) [21]. Further, a large cohort study conducted among Asian population showed FRS stratified CVD risk better than WHO risk chart did [22].

The present study reported the WHO chart can identify the highest number of people with high CVD risk compared to ACC/AHA and FRS. Hence, Iran noncommunicable disease prevention program using WHO chart provide a suitable opportunity for preventive interventions. On the other hand, CVD risk prediction in low resource countries has an important role to identify high-risk people who will benefit from the treatment. Because of limited resources, misclassification of CVD risk for primary and secondary prevention strategies is unacceptable. In spite of some studies recommending WHO risk chart for low-income countries [23], the WHO risk chart was not derived from a real cohort study [24].

In addition, the ACC/AHA risk score was reported to be suitable among Asian population without any treatment for risk factors while overestimating the risk for subjects under treatment [25]. Chia & Et al proposed FRS for CVD risk prediction in primary care among Asian population. However, a large number of study population were under treatment for risk factors which may affect the validity of the result [25]. According to our findings, the WHO risk chart found most people as high-risk group, while the best agreement was observed between FRS and ACC/AHA risk score. On the other hand, FRS was reported to be appropriate for identifying those at high risk for both CHD and CVD in Iranian people according to a population-based prospective cohort [26].

Although we presented only descriptive data on CVD risk stratification by WHO chart, FRS and ACC/AHA risk score and do not have any validation analysis data, present study have some strength deserve mentioning. First, Guilan Cohort Study comprises urban and rural population with various lifestyle factors to be representative of north of Iran. Secondly, all study data were collected and confirmed based on a national cohort study protocol. Further, we studied a large population being higher than similar previous studies in our country such as 3838 individuals in Bozorgmanesh study [26], 2103 participant in Mirzaei study [21], and 3201 individual in Motamed study [27].

Conclusion

The present study highlighted that a considerable number of the population were at moderate and high 10-year risk for CVD. The WHO risk chart stratified most individuals as high CVD risk group followed by FRS and ACC/AHA. A substantial agreement was observed between FRS and ACC/AHA, while a poor agreement was reported between WHO risk chart and FRS as well as between WHO and ACC/AHA.

Acknowledgement

We gratefully acknowledge all participants in the GCS and all staff of the Gastrointestinal and Liver Diseases Research Center along with vice-chancellor for research of Guilan University of medical sciences.

Conflict of interest: None declared.

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