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Cardiovascular Risk Prediction Models among Tunisian Diabetic Patients in the Primary Healthcare Centers of Sousse: Agreement and Sources of Discrepancies

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Abstract

Type 2 diabetes is highly prevalent in low and middle income countries including Tunisia. Two-thirds of deaths in patients with T2DM are attributable to Cardiovascular Diseases (CVD). Ordering the CVD risk was suggested to guide lifestyle modifications and pharmacological treatment prescriptions to reduce CVD incidence among diabetic people. In Tunisia, no CVD risk model was validated neither in general population nor in T2DM patients.

Aims: To evaluate the concordance between 3 models predicting the 10 years CVD risk among diabetic patients followed in primary health care centers of Sousse, Tunisia.

Methods: Cross sectional study was conducted in 2011 among diabetic patients followed in 5 randomly selected primary health care centers from the city of Sousse. Data were collected using the "Summary of Diabetes Self-Care Activities" questionnaire and the patient's clinical records. Patient's CVD risk was evaluated using the 2008-Framingham, the American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort and the Atherosclerosis Risk in Communities (ARIC) models.

Results: Patients with complete data for CVD risk prediction accounted for 136. The mean age of participants was 53.8 ± 8.1 years, 111(81.6 %) were females, 120(88.2 %) had abdominal obesity. Lack of the therapeutic targets achievement was highlighted. Contrary to the 2 other risk models, the 2008-Framingham model was applicable on all participants. Agreement between the 2008-Framingham and the ACC/AHA Pooled Cohort models were better than those between these 2 models and the ARIC model. The agreement levels between the 3 models were most important at the high risk.

Conclusion: CVD risk factors are highly prevalent among diabetic patients in the primary healthcare centers of Sousse city. The use of non calibrated risk models showed disagreement in CVD risk prediction among them. A national program of healthy lifestyle promotion should be implemented before investment in the calibration of original CVD risk scores for Tunisian general and diabetic populations.

Keywords: Cardiovascular Diseases; Type 2 Diabetes Mellitus; Primary Health Care Models; Cardiovascular-Primary Prevention

Introduction

Type 2 Diabetes Mellitus (T2DM) has became a pandemic health problem [1,2]. Its prevalence went up consistently all over the world during the past few decades, and the trend is clearly rising [3]. Two-thirds of deaths in patients with T2DM are attributable to Cardiovascular Diseases (CVD) [4]. In fact, T2DM interacts with the other CVD risk factors and multiply the CVD risk by two to four times [5, 6]. In addition, in case of developing CVD, diabetic patient's prognosis is worse compared to those without DM [4]. In fact, silent myocardial ischemia is more frequent in diabetic than in non-diabetic population [7]. Furthermore, CVD are responsible for a huge increase in both: the diabetes care expenditure and the demand for healthcare services especially in primary healthcare setting [8, 9]. In order to reduce the burden of CVD among diabetic people and to enable cost-effective use of medical resources, preventive strategies based on lifestyle modifications and preventive pharmacological treatment were suggested [5]. Several international guidelines incorporated CVD risk prediction models to identify those most likely to benefit from Aspirin and statin prescriptions [10]. However, despite the fact that most of the CVD burden is occurring in developing countries, none of the available CVD prediction models was established there [11]. On the other hand, a recent systematic review highlighted an excess of models predicting CVD with a lack of external validation and model impact studies [12]. Head to head comparison of the already existing CVD risk models and models adaptation to local settings were recommended. In Tunisia, no CVD risk engine was validated neither in general population nor in T2DM patients. Thus the aims of the current study were to evaluate the concordance between 3 models predicting 10 years CVD risk among patients with T2DM followed in the primary healthcare centers of Sousse, Tunisia and to explore the characteristics associated with the discrepancies between them.

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Methods

Study Design

Analytical cross sectional study was conducted between May 2011 and December 2011 in the primary healthcare centers of Sousse city, Tunisia among patients with T2DM. This study consists on the baseline data of a quasi-experimental study led between May 2011 and July 2012 in the same patients in order to improve their glycemic control [13].

Study Population

Patients over than 18 years, followed in the 5 randomly selected primary healthcare centers of Sousse city for T2DM, without mental or communication handicap and without history of CVD accounted for 182. Only patients with complete data for CVD risk prediction were included.

Data Collection

A trained medical doctor administered by interview the Arabic version of the Summary of Diabetes Self-Care Activities questionnaire to the participants at the primary healthcare centers. This tool covers self-care activities and healthcare provider interventions with regard to diet, physical activity, blood tests and medication [14]. The socio-demographic characteristics, the medical history, the diabetes duration, the prescribed medicines and the diabetes evolution were extracted from the patients' clinical records. Current tobacco use was self-reported and defined as having smoked at least 1 cigarette in the previous 7 days. The recommended amount of fruits and vegetables was defined as 5 or more servings per day [15]. The recommended level of physical activity as defined by WHO for adults was considered. In addition, several measurements were taken [16]. Body weight was recorded to the nearest 0.1 Kg using a portable electronic scale (PS 07, Beurer GmbH) with participants wearing a light layer of clothing. Standing height was measured with the participants in bare feet to the nearest 0.5 cm. Body Mass Index (BMI) was calculated as the patient's weight in kg divided by height in m^2. Overweight was defined as BMI of 25-29.9, and obesity was defined as BMI ≥ 30 [17].Waist to height ratio (WHtR) was calculated as the patient's waist circumference (cm) divided by its height (cm). WHtR of over 0.5 was considered as critical for an increased risk of ischemic heart disease mortality [18]. Systolic and diastolic blood pressures were measured twice using an electronic sphygmomanometer (Omron M3 Intellisense HEM-7051-E) in a seated position at rest of at least 15 minutes with the arm supported at heart level. The average of the two readings was used to assess both systolic and diastolic blood pressure. Hypertension was defined as SBP 140 mmHg or greater, DBP 90 mmHg or greater or receiving antihypertensive medication [19]. Tests in venous blood after at least 8 hours fasting were performed in the reference laboratory of primary healthcare of Sousse city. The National Cholesterol Education Program Adult Treatment Panel III criteria were used to identify dyslipidemia and metabolic syndrome among participants [20]. The suggested therapeutic targets of the American diabetes association (ADA)

were considered [19]. Ten years CVD risk was calculated online using the 3 following risk engines for each participant:

• The Atherosclerosis Risk in Communities study (ARIC) prediction model calculating the 10-year risk of heart attack or coronary heart disease risk in adults and applicable for black or white people between 45 to 65 years [21]. This model was previously suggested by the ADA and the American Heart Association (AHA) to be incorporated into the decision-making process for aspirin prescription in patients with DM [22].

• The 2008 updated Framingham model, developed in general populations with diabetes as a risk factor and which, unlike the original 1998 and revised 2002 Framingham risk models, predicts the 10 Year Risk of General Cardiovascular Disease including all of the potential manifestations and adverse consequences of atherosclerosis (Coronary heart disease death, Nonfatal myocardial infarction, Coronary insufficiency or angina, Fatal or nonfatal ischemic or hemorrhagic stroke, Transient ischemic attack, Intermittent claudication, Heart failure) for patients aged between 20 and 74 years [23]. This model was previously validated in different ethnic groups [24].

• The American College of Cardiology /American Heart Association (ACC/AHA) Pooled Cohort model, evaluates the 10-year risk of fatal coronary and non-fatal coronary events. This model is intended for use in African, American and non-Hispanic white people from 40 through 79 years of age with an LDL-cholesterol < 190 mg/dL [25]. It was developed by analyzing lengthy population-based cohort studies (including the Framingham and the ARIC studies) and was recommended to replace the 2008-Framingham risk score in the 2013 ACC/AHA guidelines [26].

These 3 risk engines were chosen because they use almost the same variables that are widely available in the primary healthcare setting in Tunisia including: the race (ARIC and ACC/AHA Pooled Cohort models), the gender, the age, the smoking status, the systolic blood pressure, the use of blood pressure lowering medication, the total cholesterol and the High Density Lipoprotein Cholesterol (HDL-C). Patients are considered to be at high risk if the predicted risk is > 10%, 20%, 7.5% using respectively the ARIC model, the 2008-Framingham model or the ACC/AHA Pooled Cohort model [22, 26-28]. They are considered to be at intermediate risk if the predicted risk is between 5% - 10%, 10% - 20% and 5% - 7.5% using the same risk models respectively [26- 28].

Statistical Analysis

SPSS for windows, version 10.0 software (SPSS Inc., Chicago, IL, USA) was used for data capture and analysis. Descriptive statistics were reported as frequencies for categorical variables and as means and standard deviations for quantitative ones. Agreement between the risk prediction scores was evaluated using the Intra Class Correlation (ICC) estimates and their 95% confident intervals calculated based on a single-rating, consistency, 2-way mixed-effects model. Values less than 0.5

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are indicative of poor agreement, values between 0.5 and 0.75 indicate moderate agreement, values between 0.75 and 0.9 indicate good agreement, and values greater than 0.90 indicate excellent agreement [29]. Overall agreement and agreement by risk level between the 3 risk engines were assessed using the Mc Nemar test and Kappa statistic (K) considering values < 0 as indicating no agreement , 0-0.20 as slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as substantial, and 0.81-1 as almost perfect agreement [30].

For univariable and multivariable analysis, 3 new variables were created in order to determine the 3 following dependent variables:

• discrepancy in ordering CVD risk between the 2008-Framingham and the ACC/AHA models ("yes" was coded as "1" and "no" was coded as "0")

• discrepancy in ordering CVD risk between the 2008-Framingham and the ARIC models ("yes" was coded as "1" and "no" was coded as "0")

• discrepancy in ordering CVD risk between the ACC/AHA and the ARIC models ("yes" was coded as "1" and "no" was coded as "0")

Besides, each dummy variable represented one category of each explanatory variable and was coded 1 if the case falls in that category and zero if not.

In the univariable analysis, the associated factors with each dependent variable were determined using the χ^2 and student-t tests when comparing percentages and means respectively. In multivariable analysis, for each dependent variable, all explanatory variables that were significant at the 20% level were included respectively in 3 binary logistic regression models. Then, a stepwise backward approach was used to select the independent variables significantly associated with each dependent variable. Results of binary logistic regression models were expressed as Odds Ratios (ORs) with confidence level of 95%. All statistical tests were 2-tailed, and p values < 0.05 were considered statistically significant.

Ethical Standards

The study was undertaken with respect for the rights and integrity of the participants. Ethical clearance was obtained from the ethical committee of Farhat Hached university hospital. Participation was voluntary and all the participants gave oral informed consent. Anonymity was insured by coding data collection sheets.

Results

Patient Characteristics

Patients with complete data for CVD risk prediction accounted for 136. The mean age of participants was 53.8 ± 8.1 years, 111 (81.6%) were females, 67 (49.3%) had hypertension, 120 (88.2 %) had abdominal obesity and 121 (89%) had metabolic syndrome (Table 1). Concerning the patient's lifestyle, 10 (7.4%)

Table 1: Cardiovascular risk profile and prognosis of diabetic patients followed in 5 primary care centers of Sousse. (n=136)

Characteristics	n (%)	Mean (SD)
Lifestyle		
Tobacco use	10(7.4)	
Practice of the recommended physical activity	45(33.1)	
5 serving fruits and vegetables intake per day	37(27.2)	
Duration of diabetes (years)		4.1(3.4)
Diabetes treatment		
Oral drugs	110(80.9)	
Insulin	4(2.9)	
Oral drugs & insulin	12(8.8)	
Sugar free diet only	10(7.4)	
Daily sugar free diet compliance	29(21.3)	
Daily diabetes medication compliance	90(66.2)	
Anthropometric measures		
BMI (Kg/m²)		31.8(9.5)
Overweight	50(36.8)	
Obesity	70(51.5)	
Waist to height ratio > 0.5	120(88.2)	
Blood pressure		
Anti-hypertension medication	67(49.3)	
SBP>140mmHg	73(53.7)	
DBP>90mmHg	39(28.7)	
Glycemic control		
Fasting plasma glucose (mmol/l)		10.7(4.9)
Glycated hemoglobin > 7%	100(73.5)	
Lipid profile		
Total cholesterol (mmol/l)		5.1(1.0)
LDL-C > 2.6 mmol/l	77(56.6)	
Low HDL-C level	24(17.6)	
TG > 1.7 mmol/l	65(47.8)	
Metabolic syndrome	121(89.0)	
10 years CVD risk prediction		
2008 Framingham model (%)		19.5(14.4)
Scores < 10%	39(28.7)	
Scores 10%-20%	48(35.3)	
Scores > 20%	49(36.0)	
ACC/AHA Pooled Cohort model (%)		10.0(10.5)

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Scores < 5%	52(38.2)	
Scores 5%-7.5%	23(16.9)	
Scores > 7.5%	51(37.5)	
Non applicable	10(7.4)	
ARIC model (%)		13.9(9.4)
Scores < 5%	9(6.6)	
Scores 5%-10%	37(27.2)	
Scores >10%	61(44.9)	
Non applicable	29(21.3)	

were tobacco user, 45 (33.1%) were practicing the recommended physical activity, 37 (27.2%) were taking the recommended amount of fruits and vegetables and 29 (21.3%) were compliant with the sugar free diet (Table 1). Regarding the achievement of the ADA therapeutic targets, 73 (53.7%) had systolic blood pressure upper than 140 mmHg, 100 (73.5%) patients had glycated hemoglobin values upper than 7%, 77 (56.5%) had LDL-C upper than 2.6 m mol/L and 65 (47.8%) had triglycerides upper than 1.7 mmol/L (Table 1).

Assessment of CVD Risk Status

Because of the difference between the 3 models regarding the intervals of age where they are applicable, CVD risk calculation was possible using the 2008-Framingham, the ACC/AHA Pooled Cohort and the ARIC models for 136 (100%), 126 (92.6%) and 107 (78.7%) patients respectively (Table 1).The mean 10-year-CVD risk scores estimated by the 3 risk models are shown in table 1. The ARIC equation identified a greater proportion of diabetic patients with high cardiovascular risk (44.8%). While the 2008-Framingham equation classified more patients at intermediate risk (35.3%) and the ACC/AHA Pooled Cohort equation classified more patients at low risk (38.2%) (Table 1).

Agreement between the 3 CVD Risk Prediction Models

The ICC estimates indicated good agreement between the 2008-Framingham and the ACC/AHA models (ICC: 0.89 [0.85-0.92]) and moderate agreements between the ARIC and both the 2008-Framingham (ICC: 0.68 [0.57-0.77]) and the ACC/AHA models (ICC: 0.73 [0.62-0.81]). The overall agreement in ordering the CVD risk was moderate between the 2008-Framingham and the ACC/AHA Pooled Cohort models (K=0.54) and fair between the ARIC model and the two other prediction tools (Table 2). At the high risk, the agreement between the 2008-Framingham equation and the ACC/AHA Pooled Cohort equation was substantial (K=0.75). While agreements between these 2 models and the ARIC model were moderate (Table 2). At the low risk, less agreement was found: it was moderate between the 2008-Framingham and the 2 other models and fair between the ACC/AHA Pooled Cohort and the ARIC equations (K=0.26) (Table 2). In classifying patients at intermediate risk, there was even less agreement: Agreements between the ACC/AHA Pooled Cohort equation and both the 2008-Framingham and the ARIC equations

were fair and the agreement between the 2008-Framingham equation and the ARIC equations was slight (K=0.17) (Table 2).

Results of the univariable analysis for the discrepancies between the 3 models are shown in table 3. After multivariable analysis, the younger age remained as a significantly associated factor to the discrepancies between the 3 prediction models. The other most influencing factors on the discrepancies between the 2008-Framingham and the ACC/AHA Pooled Cohort models were: higher diastolic blood pressure and higher LDL-C level. Those influencing the most the discrepancies between the 2008-Framingham and ARIC models were: a BMI under 30 and higher HDL-C level. While the other predictor of discrepancy between the ACC/AHA and ARIC models were female gender (Table 4).

Discussion

This study evaluated CVD risk in patients with T2DM followed in the primary healthcare centers of Sousse city using three risk assessment tools that were previously incorporated in international CVD prevention guidelines: the ARIC, the 2008-Framingham and the ACC/AHA Pooled Cohort models. High prevalence of CVD disease risk factors and lack of the therapeutic targets achievement were highlighted. Besides, compared to the 2 other risk models, the 2008-Framingham model was applicable on the greatest proportion of patients. Agreement between the 2008-Framingham and the ACC/AHA Pooled Cohort models were better than those between these 2 models and the ARIC model. The agreement levels between the 3 models were most important at the high risk.

High proportion of females was found among participants. Indeed a predominance of females among the primary healthcare users of Sousse city was highlighted in a previous study [31-34]. Concerning the control of CVD risk factors among participants, there was high prevalence of abdominal obesity and a lack of therapeutic targets achievement among them. In line with these findings, previous studies indicated poor control of major risk factors associated to abdominal obesity in the primary healthcare settings of many other countries [35]. These results illustrate the gap in CVD prevention at the primary care setting in Tunisia. The 2008-Framingham was the most applicable model to the participants and classified more patients at intermediate risk. Its greatest level of agreement was with the ACC/AHA Pooled Cohort model. The 2008-Framingham model is a well-regarded risk tool for evaluating CVD. It has been validated in multiple populations [24]. However, it was reported that it is likely to overestimate CVD risk regardless the glycemic status (normoglycemia, pre-diabetes, and diabetes) [36]. The ACC/AHA Pooled Cohort equation was designed to overcome some of the limitations of the 2008-Framingham model [26, 37]. It was based on cohorts including participants from the ARIC, the Framingham, the Coronary Artery Risk Development in Young Adults (CARDIA), the Cardiovascular Health (CHS) and Offspring studies [26]. While it has also concern about risk overestimation in addition to a temporary intermediate risk group producing [38, 39, 40].

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Table 2: Concordances and discrepancies in stratifying cardiovascular risk using 3 prediction models among diabetic patients followed in 5 primary care centers of Sousse

	2008 Framingham model				ACC/AHA Pooled cohort Model			
	Concordance	Discrepancy	p-value	K*	Concordance	Discrepancy	p-value	K*
Overall comparaison								
2008 Framingham model n(%)					87(69.05)	39(30.95)	< 0.001	0.54
ACC/AHA Pooled cohort Model n (%)	87(69.05)	39(30.95)	< 0.001	0.54				
ARIC model n (%)	63(58.87)	44(41.12)	< 0.001	0.35	59(57.84)	43(42.15)	< 0.001	0.37
Comparaison at high risk								
2008 Framingham model n(%)					111(88.1)	15(11.9)	0.6	0.75
ACC/AHA Pooled cohort Model n(%)	111(88.1)	15 (11.9)	0.6	0.75				
ARIC model n(%)	77(71.9)	30(28.1)	< 0.001	0.46	78 (76.5)	24(23.5)	0.002	0.54
Comparaison at intermediate risk								
2008 Framingham model n(%)					88(69.8)	38(30.1)	< 0.001	0.26
ACC/AHA Pooled cohort Model n(%)	88(69.8)	38(30.1)	< 0.001	0.26				
ARIC model n(%)	66(61.7)	41(38.4)	0.75	0.17	71(69.6)	31(30.3)	0.011	0.26
Comparaison at low risk								
2008 Framingham model n(%)					101(80.1)	25(19.9)	< 0.001	0.57
ACC/AHA Pooled cohort Model n(%)	101(80.1)	25(19.9)	< 0.001	0.57				
ARIC model n(%)	90(84.1)	17(15.9)	< 0.001	0.44	71(69.6)	31(30.4)	< 0.001	0.26
*: kappa statistic								

Table 3: Discrepancies in cardiovascular risk prediction between the 2008 Framingham, the ACC/AHA Pooled cohort and the ARIC models according to the characteristics of the diabetic patients followed in 5 primary care centers of Sousse

Characteristics	2008 Framingham model versus ACC/AHA Pooled Cohort model			2008 Framingham model versus ARIC model			ACC/AHA Pooled Cohort model versus ARIC model		
	Agreement	Discrepancy	p-value	Agreement	Discrepancy	p-value	Agreement	Discrepancy	p-value
Age(years) mean(SD)	55.5(8.4)	52.3(5.4)	0.012	57.7(4.4)	52.5(6.5)	0.001	57.2(5.3)	52.0(5.2)	<0.001
Female n (%)	70(80.5)	34(87.2)	0.36	41(75.9)	22(81.5)	0.571	42(71.2)	42(97.7)	0.001
Tobacco use n(%)	6(11.3)	3(12)	0.93	5(12.8)	2(11.1)	0.855	7(17.5)	-	0.027
Practice of the recommended physical activity n(%)	28(32.6)	11(28.2)	0.626	16(30.2)	9(33.3)	0.774	22(37.9)	10(23.3)	0.117
5 serving fruits and vegetables intake per day n(%)	26(30.6)	8(21.1)	0.275	19(35.8)	7(26.9)	0.428	21(36.2)	9(21.4)	0.111
Waist to Height Ratio > 0.5 n(%)	77(91.7)	34(91.9)	0.967	47(92.2)	23(88.5)	0.594	50(89.3)	38(92.7)	0.569
Obesity n(%)	43(50)	23(60.5)	0.279	33(63.5)	9(33.3)	0.011	31(53.4)	24(57.1)	0.714
Metabolic syndrome n(%)	77(88.5)	35(89.7)	0.838	49(90.7)	23(85.2)	0.453	51(86.4)	39(90.7)	0.51

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Diabetes duration>5 years n(%)	35(46.1)	11(35.5)	0.316	21(46.7)	8(38.1)	0.513	23(46.0)	15(41.7)	0.69
Treatment by insulin n(%)	9(11.1)	3(8.1)	0.617	7(13.7)	3(11.5)	0.787	9(15.8)	2((5.1)	0.107
Systolic blood pressure(mmHg) mean(SD)	14.1(2.3)	14.2(1.9)	0.83	14.9(2.1)	14.2(1.5)	0.107	14.2(2.4)	14.1(1.7)	0.825
Diastolic blood pressure(mmHg) mean(SD)	8.1(1.2)	8.7(1.3)	0.025	8.5(1.2)	8.5(1.2)	0.824	8.2(1.2)	8.4(1.2)	0.369
Glycated hemoglobin(%) mean(SD)	8.8(2.2)	9.3(2.0)	0.26	9.1(2.1)	8.8(1.6)	0.357	9.1(2.3)	8.9(1.7)	0.812
Total cholesterol(m mol/l) mean(SD)	5.0(0.9)	5.4(0.9)	0.017	5.1(1.0)	5.5(1.1)	0.143	5.0(0.9)	5.3(0.8)	0.1
LDL-C(m mol/l) mean(SD)	2.8(0.7)	3.1(0.8)	0.031	2.9(0.8)	3.2(1.2)	0.137	2.9(0.8)	3.0(0.7)	0.453
HDL-C(m mol/l) mean(SD)	1.4(0.3)	1.5(0.3)	0.048	1.3(0.4)	1.4(0.4)	0.235	1.3(0.4)	1.5(0.3)	0.003
Triglyceride(m mol/l) mean(SD)	2.0(1.3)	1.8(0.7)	0.31	2.1(1.5)	1.9(0.6)	0.406	2.0(1.4)	1.7(0.7)	0.125

Table 4: Binary logistic regression analysis for factors related to discrepancies in coronary heart disease risk prediction between the 2008-Framingham, the ACC/AHA Cohort and ARIC

	2008 Framingham model versus ACC/AHA Pooled Cohort model			2008 Framingham model versus ARIC model			ACC/AHA Pooled Cohort model versus ARIC model		
	p-value	OR	IC 95%	p-value	OR	IC 95%	p-value	OR	IC 95%
Age (year)	0.008	0.92	0.87-0.98	<0.001	0.81	0.73-0.91	< 0.001	0.8	0.72-0.89
Female	1						0.002	36.5	3.82-349.07
Male	1								
BMI>30 (Kg/m^2)	1			0.001	0.09	0.02-0.39			
BMI ≤ 30 (Kg/m^2)				1					
Diastolic blood pressure (mmHg)	0.005	1.7	1.17-2.50						
LDL-C (mmol/l)	0.009	2.19	1.21-3.90						
HDL-C (mmol/l)				0.025	8,33	1.30-53.3			

In the current study, this model was applicable to 92.6% of participants and classified more patients at low risk. Its overall concordance in ordering CVD risk with the 2008-Framingham was moderate (K=0.54) contrary to a substantial agreement at high risk. Another cross sectional study conducted in a Peruvian sample highlighted a poor overall concordance (K=0.3) between the ACC/AHA model and 2008-Framingham [41]. Cohort studies comparing these 2 models showed contradictory results. In a Saudi population for example, the ACC/AHA Pooled Cohort Risk model was more sensitive than the 2008-Framingham model in identifying patients at high risk [42]. While in Indian patients the ACC/AHA model significantly underestimates CV risk [43-45].

The use of non calibrated risk models may be the starting point of these divergences.

The ARIC model was the less applicable model to the participants (78.7%) and classified more patients at high risk. Its agreement with the 2 other models were inferior to the agreement between them. This model was previously recommended by the ADA and AHA to be used in patients with DM [20,22]. In fact diabetes specific models were suggested to be used in patients with DM instead of general population models because of a discriminatory advantage of diabetes-specific models over general population-based models for CVD risk stratification

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in diabetes [46]. However, concerns were reported about risk overestimation by the ARIC model [47]. Furthermore, there is a large variation in the reported performance of diabetes specific risk models [48]. Lack of external validation of these models was also reported in the literature [10]. Further research is required to elucidate if diabetes specific risk models have superior performance than general population models.

The younger age was found to be associated to the discrepancies between the 3 compared models. Another study found similar result highlighting that the younger age is associated to discordance between the 2008-Framingham and UKPDS models [49]. Whereas, different other characteristics were associated with the discrepancies between the 3 models such as a BMI under 30 associated to the discrepancies between the 2008-Framingham and ARIC models similarly to recent studies finding which showed that weight status is associated to a discordance between the ACC/AHA and 2008-Framingham models [50, 51]. Other characteristic found to be associated to the models discrepancies was the female gender when comparing ACC/AHA and ARIC models. In a previous study it was reported that the use of 2008-Framingham rather than a diabetes-specific engine (UKPDS) classified more women at high risk [49]. The opposite was reported in another study [52]. While no significant difference was found between the Framingham and ARIC models among men and women in a study led among multiple ethnic patients [24]. Future calibration of the proposed models should take into account these sources of disagreement.

This study reported the cardiovascular risk profile of patients with diabetes in Tunisia where diabetes is highly prevalent. It focused on primary healthcare as it is a crucial setting for non communicable diseases prevention and management. It provided information to the local clinicians about the issues of using non calibrated CVD risk prediction models. However, the performance of such models was not assessed because of the cross-sectional design. In addition, several other risk models that take into account the family history of CVD, diabetes duration, atrial fibrillation, homoscyteinemia, microalbuminuria...etc were not included to the models comparison. Nonetheless in order to control the sources of disagreement, the 3 models were selected as they use the same variables to predict the CVD risk. In addition, the selected models use data that are easily available in the primary healthcare setting of Tunisia. Finally, data related to the patient's life style were self reported and not measured objectively which could lead to under or overestimation by the participants.

In order to optimize the care of the Tunisian diabetic patients a national program of healthy lifestyle promotion should be implemented before investment in the calibration of original CVD risk scores for Tunisian general and diabetic populations. Because of the long time required to develop a Tunisian CVD prediction model in addition to resource constraints, it would be more efficient to re-calibrate one of the proposed models. This prediction tool should be then evaluated for its impact on clinical decision and CVD incidence.

Conclusion

The current study showed high prevalence of CVD disease risk factors and lack of therapeutic targets achievement among diabetic patients followed in the primary healthcare centers of Sousse city. The use of non calibrated risk models showed disagreement in CVD risk prediction among them. A national program of healthy lifestyle promotion should be implemented before investment in the calibration of original CVD risk scores for Tunisian general and diabetic populations.

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