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Original Article

Glycated haemoglobin A1c for diagnosing metabolic syndrome in Chinese workers over 35 years old in a tertiary hospital

Liyuan Zou[1*], Shuo Lin[2*], Ping Li[3], Keyi Lin[2], Fan Zhang[2], Longyi Zeng[2]

Departments of [1]Prevention and Health Care, [2]Endocrinology, [3]Gynaecology and Obstetrics, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou 510630, China. [*]Equal contributors.

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Abstract: Aims: This study aims to evaluate the use of glycated haemoglobin A1c (HbA_1c) for diagnosing metabolic syndrome (MS) in Chinese subjects aged over 35 years. Methods: We conducted a cross-sectional survey from May 2015 to Jan 2016 in a tertiary hospital, Guangzhou, China. A total of 1457 subjects (95.1%) aged over 35 years were investigated. Questionnaire survey and physical examination were performed among all participants. Blood samples were obtained to measure fasting plasma glucose (FPG), blood lipids and HbA_1c. MS was diagnosed by the criteria of International Diabetes Federation (IDF), National cholesterol education program-adult treatment panel III (ATP III) and Chinese Diabetes Society (CDS), respectively. Results: The participants had median age 45.0 (39.0-54.5) years. By using FPG ≥ 5.6 mmol/L as definition of hyperglycaemia, the prevalence of MS (IDF), MS (ATP) and MS (CDS) in the overall population was 16.5%, 18.6% and 15.6%, respectively. By using HbA_1c ≥ 39 mmol/mol (5.7%) as definition of hyperglycaemia, the prevalence of MS (IDF), MS (ATP) and MS (CDS) was 18.7%, 22.3% and 19.4%, respectively. According to MS (IDF), MS (ATP) and MS (CDS) criteria, the κ coefficients between use of FPG and HbA_1c as definition of hyperglycaemia were 0.858, 0.738 and 0.844, respectively. The optimal HbA_1c threshold with the highest level of agreement according to IDF, ATP III and CDS criteria were 6.0%, 6.2% and 5.9%, respectively. Similar results were observed in non-diabetic subjects. Conclusions: HbA_1c could be used for diagnosing MS in Chinese workers aged over 35 years in this hospital. It may be an alternative tool of FPG to identify MS in Chinese subjects over 35 years old.

Keywords: Metabolic syndrome, glycated haemoglobin A1c, diagnosis

Introduction

Metabolic syndrome (MS) is a cluster of risk factors for cardiovascular disease (CVD) and diabetes, such as obesity, dyslipidaemia, high blood pressure (BP), and hyperglycaemia [1]. Among these factors, hyperglycaemia is widely defined by the level of fasting plasma glucose (FPG) [1, 2]. Among various clinical definitions of MS, the definition of National cholesterol education program-adult treatment panel III (NCEP-ATPIII) [3] and International Diabetes Federation (IDF) [2] were widely used. In China, we used the MS definition of Chinese Diabetes Society (CDS) [4] as the diagnostic criterion. In most of MS definitions, hyperglycaemia is often define as FPG ≥ 5.6 mmol/L or with diagnosed diabetes [1-3]. In contrast, it is defined as FPG ≥ 6.1 mmol/L and (or) a 2hPG ≥ 7.8 mmol/L, and (or) previously diagnosed diabetes by the criteria of CDS [4].

Recently, the American Diabetes Association (ADA) has recommended the utility of HbA_1c for diagnosing diabetes and detecting subjects at increased risk of diabetes [5]. Studies from the American, Italian and Korean showed that HbA_1c ≥ 39 mmol/mol (5.7%) can be used instead of FPG in identifying individuals with MS, with a good agreement [6-8]. However, evidence has suggested that HbA_1c value might differ among different ethnics. Whether HbA_1c can be used in diagnosing MS in Chinese subjects is still unclear. Sun X et al. reported limited overlap and poor agreement between FPG- and HbA_1c-based (≥ 38 mmol/mol [5.7%]) diagnosis

of MS [9]. In our previous study, we found an HbA_1c threshold of 43 mmol/mol (6.1%) showed a high specificity for diagnosing MS in Chinese subjects aged over 50 years in community-based setting. The optimal HbA_1c threshold may vary according to different criteria and populations [10]. To explore whether HbA_1c could be used for diagnosing MS in Chinese, and identify the optimal HbA_1c threshold, we further evaluated the utility of HbA_1c for diagnosing MS by different criteria in a population aged over 35 years from a cross-sectional survey conducted in a tertiary hospital.

Subjects and methods

Study design and subjects

We conducted a cross-sectional survey followed a general investigation from May 2015 to Jan 2016 in the third affiliated hospital of Sun Yat-sen university, Guangzhou, Guangdong province, China. There were 1532 workers (female 62.9%) aged over 35 years in this hospital. The survey was approved by the ethics committee of the 3rd affiliated hospital of Sun Yat-sen university. Each subject gave written informed consent before investigation.

Assessment

All subjects finished a questionnaire containing information about the medical history. Each subject completed a physical examination including measurement of height, weight, waist circumference, and blood pressure. Fasting blood samples were obtained to measure blood lipids, plasma glucose and HbA_1c.

Height and weight were measured with subjects wearing light clothing and without shoes. Waist circumference (WC) was measured at the mid-point between the lower rib margin and the iliac crest. Blood pressure was measured by trained physician using a mercury sphygmomanometer at two different consecutive times at 3-5 min intervals. Plasma glucose was measured by the glucose oxidase method. HbA_1c was measured by using high performance liquid chromatography (D-10, BIO-RAD, America, reference range was 4.0-6.0%). The HbA_1c assay is certified by the National Glycohemoglobin Standardization Program (NGSP) as having documented traceability to the Diabetes Control and Complications Trial (DCCT) reference method. We measured blood lipids and Uric acid by using HITACHI 7180 (Hitachi High-Tech Science Systems Corporation, Hitachinaka-shi, Japan).

MS was diagnosed based on three definitions, the NCEP-ATP III [3] (central obesity was defined as WC ≥ 90.0 cm for men, and WC ≥ 80.0 cm for women in Chinese), Chinese Diabetes Society (CDS) [4] and International Diabetes Federation (IDF) [2] (central obesity was defined as WC ≥ 90.0 cm for men, and WC ≥ 80.0 cm for women in Chinese). In detail, the definition of MS (CDS) requires the presence of any three or more of the following five compositions [4]: (1) central obesity, define as WC ≥ 90.0 cm for men, and WC ≥ 85.0 cm for women in Chinese (2) hyperglycaemia, defined as a FPG ≥ 6.1 mmol/L and (or) a 2hPG ≥ 7.8 mmol/L, and (or) previously diagnosed diabetes; (3) hypertension, defined as SBP ≥ 130 mmHg, and (or) DBP ≥ 85 mmHg, and (or) previously diagnosed hypertension; (4) hypertriglyceridemia, defined as a serum TG ≥ 1.70 mmol/L. (5) low HDL-C, defined as a serum HDL-C less than 1.04 mmol/L. Non-diabetic subjects were defined as individuals with FPG < 7.0 mmol/l and HbA_1c < 48 mmol/mol (6.5%), and without known diabetes.

Statistical analysis

We used SPSS for windows 19.0 for data analysis. Continuous variables are presented as means (SD), and skewed variables are presented as medians (interquartile range). We tested differences in continuous variables between groups by independent t-test (assuming a normal distribution) or Mann-Whitney U-test (assuming a skewed distribution). The receiver operating characteristic curve (ROC) of HbA_1c for diagnosing MS were plotted to determine the optimal threshold. The κ statistic was calculated as a measure of agreement between the different definitions of MS. We considered a p value < 0.05 as statistically significant for a two sided test.

Results

Clinical characteristics of the study participants

A total of 1457 subjects (95.1%) participated in the survey. 1457 subjects had median age

Table 1. Clinical characteristics of study subjects

	Total	Men (n=523)	Women (n=934)	*P value*
Age	45.0 (39.0-54.5)	46.0 (40.0-55.0)	44.0 (39.0-54.0)	0.024
WC (cm)	81.9±8.7	88.2±7.0	78.3±7.5	0.000
BMI (kg/m^2)	23.15±2.69	24.20±2.64	22.57±2.55	0.000
SBP (mmHg)	122.6±13.5	128.6±11.8	119.3±13.2	0.000
DBP (mmHg)	74.7±8.5	78.5±8.0	72.6±8.1	0.000
FPG (mmol/L)	5.19±0.98	5.35±1.12	5.10±0.87	0.000
TC (mmol/L)	5.04±0.94	5.05±1.00	5.03±0.91	0.668
HDL-c (mmol/L)	1.43±0.33	1.26±0.30	1.53±0.32	0.000
TG (mmol/L)	1.31±0.83	1.60±1.06	1.14±0.61	0.000
LDL-c (mmol/L)	3.05±0.81	3.13±0.86	3.01±0.79	0.010
Uric acid (umol/L)	344.7±98.1	413.1±93.0	306.5±78.1	0.000
HbA$_1$c (mmol/mol)	37 (33-39)	37 (34-40)	36 (33-39)	0.001
(%)	5.5 (5.2-5.7)	5.5 (5.3-5.8)	5.4 (5.2-5.7)	
MS (IDF) n (%)	241 (16.5)	114 (21.8)	127 (13.6)	0.000
MS (ATP) n (%)	271 (18.6)	130 (24.9)	141 (15.1)	0.000
MS (CDS) n (%)	228 (15.6)	129 (24.7)	99 (10.6)	0.000

WC waist circumference, BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, FPG Fasting plasma glucose, TC total cholesterol, HDL-c high density lipoprotein cholesterol, TG Triglyceride, LDL-c low-density lipoprotein cholesterol. MS metabolic syndrome, IDF International Diabetes Federation, ATP Adult Treatment Panel III, CDS Chinese Diabetes Society, HbA$_1$c Glycated hemoglobin A1c.

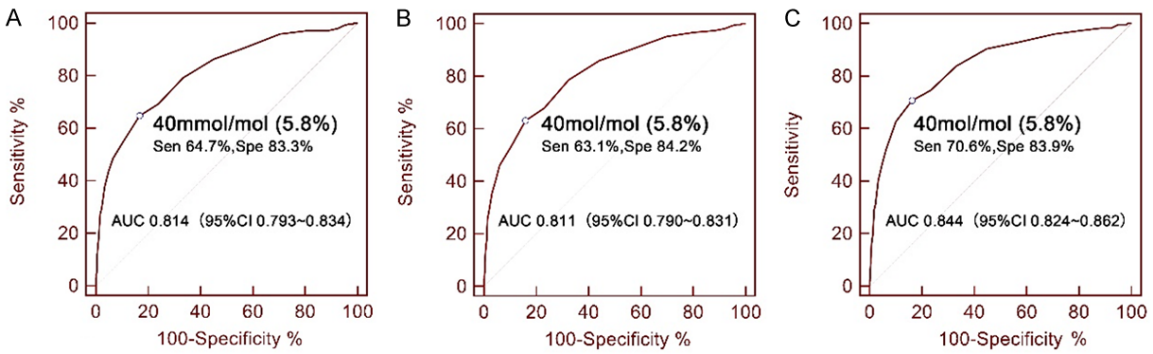

Figure 1. Receiver operating characteristic curves of HbA$_1$c for identifying metabolic syndrome by different criteria in subject over 35 years old (n=1457). A. MS (IDF). B. MS (ATP III), C. MS (CDS).

45.0 (39.0-54.5) years, mean BMI 23.2±2.7 kg/m^2, mean FPG 5.2±1.0 mmol/L, median HbA$_1$c 37 mmol/mol (33-39 mmol/mol) (5.5% [5.2-5.7%], and were 64.1% female (**Table 1**). Men were older, had higher levels of BMI, WC, SBP, DBP, TG, LDL-cholesterol, uric acid, FPG and HbA$_1$c, and had lower levels of HDL-cholesterol (all $P < 0.05$). The prevalence of MS (IDF), MS (ATP) and MS (CDS) in men was 21.8%, 24.9% and 24.7%, while the prevalence of MS (IDF), MS (ATP) and MS (CDS) was 13.6%, 15.1% and 10.6%, respectively. The prevalence of MS in men was higher than that in women irrespective of MS diagnostic criteria (all $P < 0.001$).

Diagnostic accuracy and optimal cut-points of HbA$_1$c for diagnosing MS by different criteria in the overall population and non-diabetic subjects

ROC curves were plotted to analyze the optimal HbA$_1$c cutoffs for identifying MS with IDF, NCEP ATPIII, CDS definitions (**Figure 1**). In the overall population, by using IDF definition, the area under the curves (AUC) of HbA$_1$c for diagnosing MS (IDF) were 0.814 (95% CI: 0.793~0.834). HbA$_1$c ≥ 40 mmol/mol (5.8%) (sensitivity 64.7%, specificity 83.3%) were the optimal cut-off points for determining subjects with MS. By using ATP III criterion, the AUC of HbA$_1$c for MS

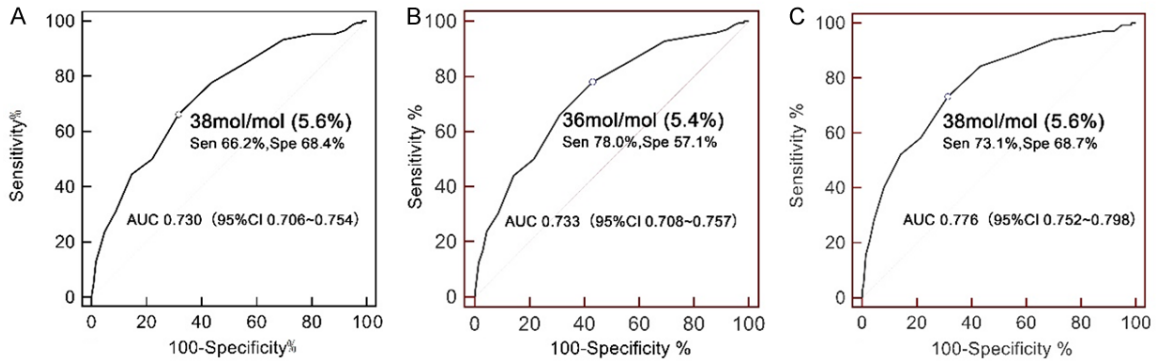

Figure 2. Receiver operating characteristic curves of HbA$_1$c for identifying metabolic syndrome by different criteria in non-diabetic subjects (n=1330). A. MS (IDF), B. MS (ATP III), C. MS (CDS).

Table 2. Impact of prevalence of metabolic syndrome for fasting plasma glucose and HbA$_1$c cut-points

Cut-points mmol/mol (%)	MS (IDF) n (%), κ*		MS (ATP) n (%), κ*		MS (CDS) n (%), κ*	
	Total n=1457	Non-DM n=1330	Total n=1457	Non-DM n=1330	Total n=1457	Non-DM n=1330
FPG ≥ 5.6 mmol/l	241 (16.5)	148 (11.1)	271 (18.6)	168 (12.6)	228 (15.6)	134 (10.1)
	-	-	-	-	-	-
HbA$_1$c ≥ 38	289 (19.8)	196 (14.7)	347 (23.8)	245 (18.4)	295 (20.2)	202 (15.2)
(5.6)	0.848	0.780	0.800	0.724	0.826	0.749
HbA$_1$c ≥ 39	273 (18.7)	180 (13.5)	325 (22.3)	224 (16.8)	282 (19.4)	189 (14.2)
(5.7)	0.858	0.792	0.738	0.738	0.844	0.772
HbA$_1$c ≥ 40	257 (17.6)	167 (12.6)	297 (20.4)	199 (15.0)	260 (17.8)	168 (12.6)
(5.8)	0.869	0.816	0.843	0.788	0.882	0.828
HbA$_1$c ≥ 41	241 (16.5)	153 (11.5)	272 (18.7)	178 (13.4)	230 (15.8)	140 (10.5)
(5.9)	0.881	0.839	0.821	0.821	0.912	0.878
HbA$_1$c ≥ 42	225 (15.4)	139 (10.5)	250 (17.2)	160 (12.0)	211 (14.5)	125 (9.4)
(6.0)	0.898	0.871	0.861	0.861	0.895	0.867
HbA$_1$c ≥ 43	219 (15.0)	133 (10.0)	240 (16.5)	150 (11.3)	199 (13.7)	115 (8.6)
(6.1)	0.897	0.869	0.857	0.857	0.882	0.854
HbA$_1$c ≥ 44	210 (14.4)	127 (9.5)	229 (15.7)	142 (10.7)	187 (12.8)	107 (8.0)
(6.2)	0.893	0.874	0.869	0.869	0.874	0.859
HbA$_1$c ≥ 45	196 (13.5)	116 (8.7)	215 (14.8)	131 (9.8)	173 (11.9)	96 (7.2)
(6.3)	0.879	0.866	0.861	0.861	0.841	0.820
HbA$_1$c ≥ 46	194 (13.3)	114 (8.6)	212 (14.6)	128 (9.6)	171 (11.7)	94 (7.1)
(6.4)	0.873	0.856	0.848	0.848	0.835	0.809

*κ value represent for diagnostic agreement between use of FPG and HbA$_1$c as definition of hyperglycaemia for diagnosing MS. MS metabolic syndrome, IDF International Diabetes Federation, ATPIII Adult Treatment Panel III, CDS Chinese Diabetes Society, HbA$_1$c Glycated hemoglobin A1c.

(CDS) was 0.811 (95% CI: 0.790~0.831). The optimal cut-off points of HbA$_1$c were 40 mmol/mol (5.8%), with a sensitivity of 63.1% and a specificity of 84.2%. With CDS definition, the AUC of HbA$_1$c for MS (CDS) was 0.844 (95% CI: 0.824~0.862). The optimal cut-off points of HbA$_1$c were 40 mmol/mol (5.8%), with a sensitivity of 70.6% and a specificity of 83.9% (**Figure 1**).

The ROC curves of HbA$_1$c in diagnosing MS for non-diabetic subjects (n=1330) are shown in **Figure 2**. By using IDF definition, the AUC of HbA$_1$c for diagnosing MS (IDF) were 0.730 (95%

Table 3. Distributions of metabolic syndrome by different HbA_1c cut-points as definition of hyperglycaemia in overall population (n=1457)

HbA_1c mmol/mol (%)	MS (IDF), n (%)*			MS (ATP), n (%)*			MS (CDS), n (%)*		
	FPG only	HbA_1c only	FPG and HbA_1c	FPG only	HbA_1c only	FPG and HbA_1c	FPG only	HbA_1c only	FPG and HbA_1c
≥ 38 (5.6)	9 (3.7)	57 (23.7)	232 (96.3)	11 (4.1)	87 (32.1)	260 (95.9)	4 (1.8)	71 (31.1)	224 (98.2)
≥ 39 (5.7)	14 (5.8)	46 (19.1)	227 (94.2)	18 (6.6)	72 (26.6)	253 (93.4)	6 (2.6)	60 (26.3)	222 (97.4)
≥ 40 (5.8)	19 (7.9)	35 (14.5)	222 (92.1)	23 (8.5)	49 (18.1)	248 (91.5)	8 (3.5)	40 (17.5)	220 (96.5)
≥ 41 (5.9)	24 (10.0)	24 (10.0)	217 (90.0)	31 (11.4)	32 (11.8)	240 (88.6)	16 (7.0)	18 (7.9)	212 (93.0)
≥ 42 (6.0)	28 (11.6)	12 (5.0)	213 (88.4)	37 (13.7)	16 (5.9)	234 (86.3)	28 (12.3)	11 (4.8)	200 (87.7)
≥ 43 (6.1)	31 (12.9)	9 (3.7)	210 (87.1)	42 (15.5)	11 (4.0)	229 (84.5)	36 (15.8)	7 (3.1)	192 (84.2)
≥ 44 (6.2)	36 (14.9)	5 (2.1)	205 (85.1)	47 (17.3)	5 (1.8)	224 (82.7)	43 (18.9)	2 (0.9)	185 (81.1)

*The percentage in parenthesis is calculated by the former number divided by the number of subjects with MS identified by using FPG ≥ 5.6 mmol/L (the number of "FPG only" + the number of "FPG and HbA_1c") as definition of hyperglycaemia. MS metabolic syndrome, IDF International Diabetes Federation, ATP Adult Treatment Panel III, CDS Chinese Diabetes Society, HbA_1c Glycated hemoglobin A1c, FPG fasting plasma glucose.

CI: 0.706~0.754). HbA_1c ≥ 38 mmol/mol (5.6%) (sensitivity 66.2%, specificity 68.4%) were the optimal cut-off points for determining subjects with MS. By using ATP III definition, the AUC of HbA_1c for diagnosing MS (ATP) were 0.733 (95% CI: 0.708~0.757). HbA_1c ≥ 37 mmol/mol (5.5%) (sensitivity 78.0%, specificity 57.1%) were the optimal cut-off points for determining subjects with MS. With CDS definition, the AUC of HbA_1c for MS (CDS) was 0.776 (95% CI: 0.752~0.798). The optimal cut-off points of HbA_1c were 38 mmol/mol (5.6%), with a sensitivity of 73.1% and a specificity of 68.7% (**Figure 2**).

HbA_1c instead of fasting plasma glucose as definition of hyperglycaemia for identifying MS by different criteria

The impact of HbA_1c instead of FPG as *definition of hyperglycaemia* for diagnosing MS are shown in the **Table 2**. In the overall population, by using HbA_1c ≥ 39 mmol/mol (5.7%) as definition of hyperglycaemia, the prevalence of MS (IDF), MS (ATP) and MS (CDS) were 18.7%, 22.3%, and 19.4%, respectively (with agreement of 95.9%, 93.8%, and 95.5%, respectively). The corresponding κ values were 0.858, 0.738 and 0.844, respectively. By using HbA_1c ≥ 42 mmol/mol (6.0%) as hyperglycaemia criterion, the prevalence of MS (IDF) was 15.4% (with a highest κ value of 0.898). By using HbA_1c ≥ 44 mmol/mol (6.2%) as hyperglycaemia criterion, the prevalence of MS (ATP) was 9.5% (with a highest κ value of 0.874). By using HbA_1c ≥ 41 mmol/mol (5.9%) as hyperglycaemia criterion, the prevalence of MS (CDS) was 15.8% (with a highest κ value of 0.912).

Table 3 shows the distributions of MS by using different HbA_1c cut-points as definition of hyperglycaemia for diagnosis of MS in overall population. By using HbA_1c ≥ 39 mmol/mol (5.7%) as definition of hyperglycaemia, additional 19.1-26.6% of MS subjects could be detected according to different MS criteria.

Among the non-diabetic subjects (**Table 2**), by using HbA_1c ≥ 39 mmol/mol (5.7%) as definition of hyperglycaemia, the prevalence of MS (IDF), MS (ATP) and MS (CDS) were 13.5%, 16.8%, and 14.2%, respectively (with agreement of 95.4%, 93.4%, and 95.1%, respectively). The corresponding κ values were 0.792, 0.738 and 0.772, respectively. By using HbA_1c ≥ 44 mmol/mol (6.2%) as hyperglycaemia criterion, the prevalence of MS (IDF) was 9.5% (with the highest κ value of 0.874). By using HbA_1c ≥ 38 mmol/mol (6.2%) as hyperglycaemia criterion, the prevalence of MS (ATP) was 10.7% (with the highest κ value of 0.869). By using HbA_1c ≥ 41 mmol/mol (5.9%) as hyperglycaemia criterion, the prevalence of MS (CDS) was 10.5% (with a highest κ value of 0.878).

Discussion

In the present study, according to ROC curves, an HbA_1c ≥ 40 mmol/mol (5.8%) was the optimal threshold for diagnosing MS by using definition of ATP-III, CDS and IDF in the overall population, with AUCs varied from 0.814 to 0.844. By using HbA_1c as criterion of hyperglycaemia, HbA_1c cut-points of 41-44 mmol/mol (5.9-6.2%) showed the highest κ value from 0.874 to 0.912 and good agreements by different definition of MS. Similar results were observed

among non-diabetic subjects, while an $HbA_1c \geq 38$ mmol/mol (5.6%) was the optimal threshold for diagnosing MS by using definition of ATP-III, CDS and IDF. Our results suggested HbA_1c may be a useful tool to identify MS in Chinese subjects over 35 years.

While ADA recommended the use of HbA_1c for diagnosis of diabetes and subjects with increased diabetes risk. Several studies reported the impact of HbA_1c instead of FPG to define MS [6, 8, 9, 11, 12]. A study conducted in non-diabetic Italian reported a higher prevalence of MS by using HbA_1c than by FPG (42.1% vs 39.7%) [8]. Xingxing Sun et.al also reported a higher prevalence of MS define by $HbA_1c \geq 38$ mmol/mol than that by FPG $\geq$ 5.6 mmol/l (21.5% vs 14.9%, respectively) in Chinese participants aged $\geq$ 18 years from the China Health and Nutrition Survey 2009 [9]. In contrast, studies in American and Korean reported a lower prevalence of MS by using $HbA_1c \geq 38$ mmol/mol than by FPG $\geq$ 5.6 mmol/l [6, 11]. These results also suggested HbA_1c-based diagnosis of MS illustrated limited overlap with FPG-based diagnosis of MS. In accordance with studies in Italian and Chinese, our study suggested that by $HbA_1c \geq 38$ mmol/mol as criteria of dsyglycemia for identifying MS would increase the prevalence of MS, irrespective of different criteria in the study population. This may be partly explained as a large proportion of Chinese with isolated postprandial hyperglycaemia [13]. While the HbA_1c cut-point increase, the prevalence of MS decline and the diagnostic agreement increased. The optimal threshold which showed a highest κ value ranged from 41-44 mmol/mol (5.9-6.2%), depending on the specific criteria. The optimal cut-points were higher than 39 mmol/mol (5.7%). Combined with other studies, all these results indicated 39 mmol/mol (5.7%) may not suitable for Chinese to identify MS. However, different cut-points were reported in different researches may due to different populations and diagnostic criteria. Further prospective studies need to be conducted to explore the optimal cut-points for specific population.

The limited overlap between HbA_1c- and FPG-based diagnosis of MS reflect different facets of glucose metabolism [14, 15]. While FPG offered daily preprandial glucose snapshot, HbA_1c represents chronic exposure to fasting and postprandial hyperglycaemia [14, 15]. Therefore, the HbA_1c-based definition of MS reflects more of the postprandial glucose-based diagnosis of MS. In the present study, by using $HbA_1c \geq 38$ mmol/mol (5.7%) as definition of hyperglycaemia, the agreement of MS diagnosed by FPG and HbA_1c was 93.8-95.9%, and using HbA_1c could detect additional 19.1-26.6% of MS subjects according to different MS criteria. The agreement of FPG-based and HbA_1c-based diagnosis of MS in the present study was better than those of other results. It is possible that how well HbA_1c performs as compared with FPG for the diagnosis of MS will depend on different population and assay of HbA_1c. In our study, HbA_1c instead of FPG for diagnosis of MS showed a good agreement. Given that HbA_1c is easy to use, with less variability, no need for fasting, and is a good index to predict future risk of cardiovascular diseases [16-18], HbA_1c may be a useful tool for diagnosis of MS. Specific cut-points among different populations need to be determined in the further studies.

As previous studies showed mixed results as to whether the presence of MS increased cardiovascular risks in subjects with diabetes [19-21], we repeated the analysis in subjects without diabetes. In our study, HbA_1c showed less agreement for diagnosing MS in non-diabetic subjects than that in the overall population. However, $HbA_1c \geq 38$ mmol/mol presented with agreement of 93.4-95.5% and κ values ranged from 0.738 to 0.844, and HbA_1c cut-points of 41-44 mmol/mol (5.9-6.2%) showed the highest κ value ranged from according to different MS criteria. In line with other studies [10, 11, 22-25], our results suggested HbA_1c was a useful tool for diagnosing MS in non-diabetic subjects.

Our study adds to the literature by demonstrating that HbA_1c could be used as a valuable tool for identifying MS in a large Chinese cohort. The strength of our study was exploring the impact of HbA_1c for diagnosing MS by different diagnostic criteria, both in overall population or non-diabetic subjects. There were some limitations in our study. First, our study only investigated hospital workers over 35 years old in China, which may restrict the application of our conclusion. Further studies need to be conducted in other Chinese population. Second, the present study is a cross-sectional study, so

we couldn't explore the ability of HbA_1c for predicting cardio-vascular diseases. We need further prospective cohort studies to evaluate the use of HbA_1c for predicting cardio-vascular events.

In conclusion, HbA_1c could be used for diagnosing MS in Chinese workers aged over 35 years in this hospital. It may be an alternative tool of FPG to identify Chinese subjects of over 35 years old with metabolic syndrome.

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Disclosure of conflict of interest

None.

Address correspondence to: Longyi Zeng, Department of Endocrinology, The 3rd Affiliated Hospital of Sun Yat-sen University, No. 600, Tianhe Lu, Guangzhou 510630, China. Tel: +86 02085253408; E-mail: zengly@mail.sysu.edu.cn

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