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An innovative prognostic model for predicting diabetes risk in the Thai population

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ABSTRACT

Objective: To estimate the prevalence and type 2 diabetes, and to develop a prognostic model for identifying individuals at high risk of undiagnosed type 2 diabetes.
Research design and methods: The study was designed as a cross-sectional investigation with 4314 participants of Thai background, aged between 15 and 85 years (mean age: 48). Fasting plasma glucose was initially measured, and repeated if the first measurement was more than 126 mg/dl. Type 2 diabetes was diagnosed using the World Health Organization's criteria. Logistic regression model was used to develop prognostic models for men and women separately. The prognostic performance of the model was assessed by the area under the receiver operating characteristic curve (AUC) and a nomogram was constructed from the logistic regression model.
Results: The overall prevalence of type 2 diabetes was 7.4% (n = 125/1693) in men and 3.4% (n = 98/2621) in women. In either gender, the prevalence increased with age and body mass index (BMI). Gender, age, BMI and systolic blood pressure (SBP) were independently associated with type 2 diabetes risk. Based on the estimated parameters of model, a nomogram was constructed for predicting diabetes separated by gender. The AUC for the model with 3 factors was 0.75.
Conclusions: These data suggest that the combination of age, BMI and systolic blood pressure could help identify Thai individuals at high risk of undiagnosed diabetes.

1. Introduction

Type 2 diabetes is increasingly recognized as a public health burden in developing countries [1,2]. Recent studies have suggested that the prevalence of type 2 diabetes in Asian populations ranged between 6 and 12% [1,3–5], which is comparable to estimates from Caucasian populations in the US [6]. Indeed, it has been projected that a large increase in the global prevalence of diabetes will take place in developing countries with 80% of all new cases of diabetes expected to appear in the developing countries by 2025 [7]. The Asia-Pacific region, including Thailand, has been identified as of "prime importance to the epidemiology of diabetes" [8] because the prevalence of diabetes in this part of the world is higher than in other developing countries [9].

One of the most significant current discussions in diabetes is how to identify individuals at high risk of having the disease. A large proportion of diabetic cases are undiagnosed (e.g., asymptomatic), yet these individuals are at risk of having serious adverse outcomes, including cardiovascular diseases and mortality. Therefore, there is an urgent need for predictive models to identify high-risk individuals for early intervention.

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A number of prognostic models have been developed for predicting the risk of diabetes in Caucasians, but few are available for Asian populations [10–13]. It is not clear whether these models can be applied to different populations where prevalence and risk factors might be different from the populations where the tools were developed. Moreover, most previous models were based on the concept of risk stratification, in which continuous variables were categorized into subgroups, whereas our model was based on the concept of individualization, in which the continuous nature of risk factors were preserved in order to increase the degree of uniqueness of an individual.

In this study, we sought to estimate the prevalence of undiagnosed type 2 diabetes, and to develop simple prognostic models for identifying high-risk individuals in primary care setting.

2. Study design and methods

2.1. Setting and subjects

The study was designed as a cross-sectional investigation, with the setting being Khon Kaen, a northeast rural province of Thailand (about 445 km from Bangkok). The province has a population of 1.8 million, living mostly in rural areas. The setting was a health check-up clinic of the Srinagarind Hospital, which is a teaching hospital of the University of Khon Kaen. Although the clinic was set up to serve the entire provincial population, the majority of clients who visit the clinic lived around the capital city of the province.

The study was formally approved by the Ethics Committee of Khon Kaen University and written informed consent was obtained from each individual. From 2003 to 2004, all men and women who came to the clinic for health check-up were invited to provide basic clinical information for the study. A total of 4314 participants (1693 men and 2621 women) were included in the study. All participants were of Thai background and were excluded from analysis if they were taking medications for hypertension, diabetes, or dyslipidemia.

2.2. Measurements

The participants were invited to meet with a research nurse who completed a questionnaire and an informed consent form. Body weight (including light indoor clothing) was measured using an electronic balance (accuracy 0.1 kg) and standing height (without shoes) using a stadiometer (nearest 0.1 cm). Body mass index (BMI) was calculated the ratio of weight in kg divided by height in m^2. Systolic blood pressure (SBP) was measured twice in the left arm and recorded after a participant had been seated and rest for 5 min. The average of the two measurements was then used for all analyses. Diastolic blood pressure (DBP) was recorded at the fifth Korotkoff sound. Hypertension was defined as a systolic blood pressure of at least 140 mmHg and/or a diastolic blood pressure of at least 90 mmHg.

Serum samples were collected in the morning after a participant had fasted for 12 h prior to the clinic visit. Blood samples were immediately centrifuged. Measurements included fasting plasma glucose (FPG), total cholesterol, triglycerides. Fasting plasma glucose levels were measured the glucose oxidase method. Serum total cholesterol and triglyceride were measured by enzymatic methods using an automatic autoanalyzer (Cobas Integra 800; Roche Diagnostics, Mannheim, Germany). The diagnosis of diabetes was based on the WHO's criteria using FPG $\geq$126 mg/dl and repeated within 1 week.

2.3. Statistical analyses

In order to develop an optimal model for predicting diabetes risk, the linear logistic regression models were considered. Given many potential risk factors for diabetes, the number of possible models can be very large. The Bayesian Model Average (BMA) method [14] was applied to search for the most parsimonious models with consistent and maximum discriminatory power. In terms of model consistency and accuracy, it has been shown that the BMA approach performed better than traditional algorithms such as stepwise regression [15,16], because it can account for model uncertainty in both predictions and parameter estimates [14,17]. The prognostic performance of model was assessed by the area under the receiver operating characteristic curve (AUC). Based on the test, an optimal model was selected, and parameter estimates of this model were then used for constructing a nomogram using the Design library [18]. The bootstrap method was applied to examine the predictive accuracy of the nomogram in new settings. In this method, subsamples, each with 150 men and women, were repeatedly resampled (with replacement) from the original entire dataset, and parameter estimates were computed for each subsample and were used for the calibration of predictive accuracy [19].

3. Results

A total of 4314 Thai participants, aged between 15 and 85 years (mean age: 49.4 and 47 years for men and women, respectively) were included in this study. Men had a heavier, taller, and higher BMI than women. Both SBP and DBP, FPG and triglyceride levels were also significantly higher in men than in women (Table 1).

The prevalence of diabetes of all participants was 5.2% (n = 223/4314), with 7.4% in men and 3.7% in women. As expected, diabetic men and women were, on average, older, heavier, higher BMI, higher SBP and DBP than those without diabetes. Furthermore, total cholesterol and triglyceride levels were significantly higher in the both men and women with diabetes compared to the non-diabetes group (data not shown). The prevalence of diabetes increased with advancing age and higher BMI in both men and women (Table 2).

Being man, advancing age, higher BMI and SBP were each significantly and independently associated with an increased risk of diabetes (Table 3). The odds of having diabetes was increased by 1.3 (95% CI: 1.2–1.4) for each 5-year increased in age; 1.1 (95% CI: 1.07–1.14) for each 1-kg/m^2 increased in BMI, and 1.1 (95% CI: 1.03–1.20) for each 10-mmHg increased in SBP. Moreover, men had greater odds of diabetes than women (OR 1.8; 95% CI: 1.4–2.4). The AUC for the model was 0.753 (95%

Table 1 – Characteristics of study subjects.

Variable	Women	Men	P-value
N	2621	1693	
Age (year)	47.0 ± 10.4	49.4 ± 11.0	<0.0001
Weight (kg)	56.9 ± 9.3	67.4 ± 10.4	<0.0001
Height (cm)	155.1 ± 5.6	165.5 ± 5.8	<0.0001
BMI (kg/m^2)	23.7 ± 3.8	24.6 ± 3.5	<0.0001
BMI ≥25 kg/m^2 (%)	31.2	42.3	<0.0001
BMI > 30 kg/m^2 (%)	6.1	5.9	<0.001
Systolic blood pressure (mmHg)	117.3 ± 16.4	121.9 ± 16.3	<0.0001
Diastolic blood pressure (mmHg)	76.2 ± 10.9	80.4 ± 11.0	<0.0001
Hypertension (%)	21.7	32.3	<0.0001
Fasting blood glucose (mg/dl)	88.8 ± 20.6	96.1 ± 31.0	<0.0001
Total cholesterol (mg/dl)	211.2 ± 42.5	212.6 ± 43.6	0.3151
Triglyceride (mg/dl)	115.7 ± 76.1	163.2 ± 118.9	<0.0001

Notes: Unless otherwise stated, data are shown as mean ± stan- standard deviation. *P*-values were derived from *t*-test (for continuous data) or Chi-square test (for categorical data) for difference between men and women.

Table 2 – Prevalence of DM by age, sex and BMI category.

Strata	Women		Men		P-value
	Frequency[a]	%	Frequency[a]	%	
Age group					
14–39	4/616	0.7	7/303	2.3	0.0295
40–49	24/1038	2.3	35/622	5.6	0.0004
50–59	38/631	6.0	41/429	9.6	0.0315
60+	32/336	9.5	42/339	12.4	0.2335
Total	98/2621	3.7	125/1693	7.4	<0.0001
BMI group					
<23	25/1280	1.9	25/547	4.6	0.0017
23–25	23/530	4.3	31/435	7.1	0.0609
25–30	39/650	6.0	52/612	8.5	0.0866
>30	11/161	6.8	17/99	17.2	0.0090

P-values were derived from Chi-square test (for categorical data) for difference between men and women.
[a] Frequency is represented by the number of DM cases over total sample size.

Table 3 – Risk factors for undiagnosed type 2 diabetes.

Risk factors	Odds ratio and 95% confidence interval	P-value
Gender (men)	1.79 (1.35–2.36)	<0.0001
Age (per 5 years)	1.29 (1.20–1.38)	<0.0001
Body mass index (per 1 kg/m^2)	1.10 (1.07–1.14)	<0.0001
Systolic blood pressure (per 10 mmHg)	1.11 (1.03–1.20)	0.009

confidence interval: 0.712–0.775). The Hosmer–Lemeshow calibration test result was 8.04 ($P = 0.43$).

Based on the parameter estimates of model, the probability of having diabetes (denoted by p) was estimated by the following equation: $p = 1/(1 + \exp(-x))$, where $x = -8.857 + 0.0506 \times Age + 0.0948 \times BMI + 0.0106 \times SBP$ for men, and $x = -9.437 + 0.0506 \times Age + 0.0948 \times BMI + 0.0106 \times SBP$ for women. If a probability of diabetes of at least 0.10 is considered high-risk, then according

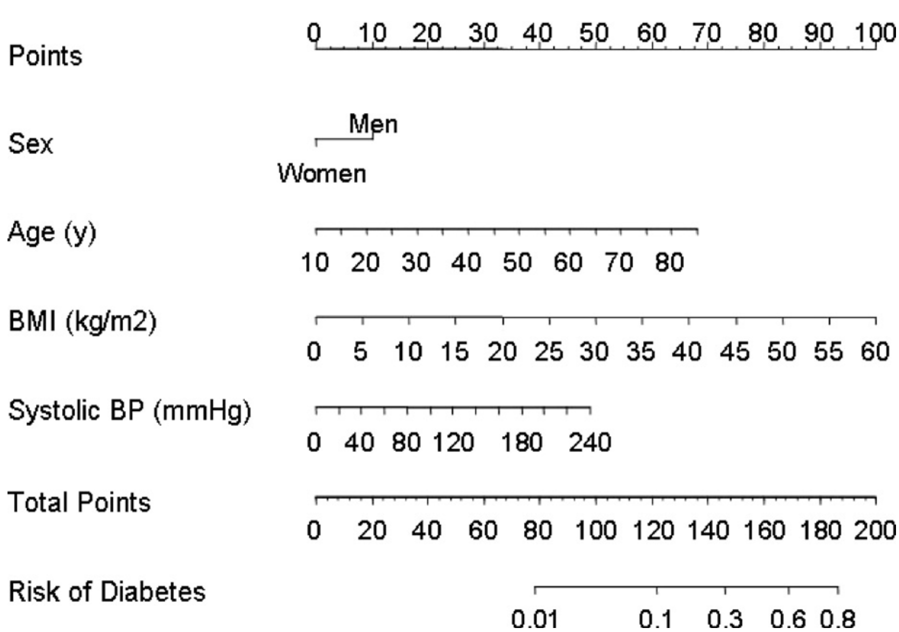

Fig. 1 – Nomogram for predicting diabetes in Thai men and women. *Instruction for usage*: Mark an individual's age on the "Age" axis, and draw a vertical line to the "Point" axis to determine the number of points the individual receives for her age. Repeat this process for the BMI and SBP. Add the number of points from each predictor. Mark this sum on the "Total Points" axis, and draw a vertical line down to meet the "Risk of Diabetes" axis, to find the woman's probability of having diabetes. *Example*: Mrs. X, 50 years old, BMI 30 kg/m^2 and has SBP 160 mmHg; her points for age is approximately 37, her BMI points is 50; and SBP points is 33 Her total points is therefore 37 + 50 + 33 = 120, and the probability of having diabetes is around 0.09. In other words, in 100 women like her, 9 will have diabetes.

to this model, virtually all men age 50+ years, BMI 35+ and with SBP of 100 or more are in the high-risk group whereas all women age 50+ years, BMI 40+ and with SBP of 100 or more are in the high-risk group (Table 4).

Based on the regression coefficients, a nomogram for predicting diabetes risk was constructed (Fig. 1). For example, a woman aged 50 years, BMI 30 kg/m^2, with SBP 160 mmHg, is predicted to have a 9% chance of having diabetes. However, with the same BMI and the same SBP, a man aged 70 years would have a probability of diabetes of approximately 32%.

4. Discussion

Although public burden of diabetes in Asia is increasingly recognized, there have been very few studies of diabetes in

Table 4 – Predicted probability of having diabetes for a given age, BMI and SBP by gender.

Age (year)	BMI (kg/m^2)	Systolic blood pressure (mmHg)								
		100	110	120	130	140	150	160	170	180
Men										
30	20	0.01	0.01	0.02	0.02	0.02	0.02	0.02	0.03	0.03
	25	0.02	0.02	0.02	0.03	0.03	0.03	0.04	0.04	0.04
	30	0.03	0.03	0.04	0.04	0.05	0.05	0.06	0.06	0.07
	35	0.05	0.05	0.06	0.07	0.07	0.08	0.09	0.10	0.11
	40	0.08	0.08	0.09	0.10	0.11	0.12	0.14	0.15	0.16
40	20	0.02	0.02	0.02	0.03	0.03	0.03	0.04	0.04	0.05
	25	0.03	0.04	0.04	0.04	0.05	0.05	0.06	0.07	0.07
	30	0.05	0.06	0.06	0.07	0.08	0.08	0.09	0.10	0.11
	35	0.08	0.09	0.10	0.11	0.12	0.13	0.14	0.15	0.17
	40	0.12	0.13	0.15	0.16	0.17	0.19	0.21	0.22	0.24
50	20	0.03	0.04	0.04	0.05	0.05	0.06	0.06	0.07	0.07
	25	0.05	0.06	0.06	0.07	0.08	0.09	0.09	0.10	0.11
	30	0.08	0.09	0.10	0.11	0.12	0.13	0.14	0.16	0.17
	35	0.12	0.14	0.15	0.16	0.18	0.19	0.21	0.23	0.25
	40	0.19	0.20	0.22	0.24	0.26	0.28	0.30	0.32	0.35
60	20	0.05	0.06	0.07	0.07	0.08	0.09	0.10	0.11	0.12
	25	0.08	0.09	0.10	0.11	0.12	0.13	0.15	0.16	0.18
	30	0.13	0.14	0.15	0.17	0.18	0.20	0.22	0.24	0.26
	35	0.19	0.21	0.23	0.25	0.27	0.29	0.31	0.33	0.36
	40	0.28	0.30	0.32	0.34	0.37	0.39	0.42	0.44	0.47
70	20	0.09	0.10	0.10	0.11	0.13	0.14	0.15	0.17	0.18
	25	0.13	0.14	0.16	0.17	0.19	0.21	0.22	0.24	0.26
	30	0.20	0.21	0.23	0.25	0.27	0.29	0.32	0.34	0.36
	35	0.28	0.30	0.33	0.35	0.37	0.40	0.43	0.45	0.48
	40	0.39	0.41	0.44	0.46	0.49	0.52	0.54	0.57	0.60
Women										
30	20	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.02
	25	0.01	0.01	0.01	0.02	0.02	0.02	0.02	0.02	0.03
	30	0.02	0.02	0.02	0.02	0.03	0.03	0.03	0.04	0.04
	35	0.03	0.03	0.03	0.04	0.04	0.05	0.05	0.06	0.06
	40	0.04	0.05	0.05	0.06	0.07	0.07	0.08	0.09	0.10
40	20	0.01	0.01	0.01	0.02	0.02	0.02	0.02	0.02	0.03
	25	0.02	0.02	0.02	0.02	0.03	0.03	0.03	0.04	0.04
	30	0.03	0.03	0.04	0.04	0.04	0.05	0.05	0.06	0.07
	35	0.05	0.05	0.06	0.06	0.07	0.08	0.08	0.09	0.10
	40	0.07	0.08	0.09	0.10	0.11	0.12	0.13	0.14	0.15
50	20	0.02	0.02	0.02	0.03	0.03	0.03	0.04	0.04	0.04
	25	0.03	0.03	0.04	0.04	0.05	0.05	0.06	0.06	0.07
	30	0.05	0.05	0.06	0.06	0.07	0.08	0.09	0.09	0.10
	35	0.07	0.08	0.09	0.10	0.11	0.12	0.13	0.14	0.16
	40	0.11	0.12	0.14	0.15	0.16	0.18	0.19	0.21	0.23
60	20	0.03	0.03	0.04	0.04	0.05	0.05	0.06	0.06	0.07
	25	0.05	0.05	0.06	0.07	0.07	0.08	0.09	0.10	0.11
	30	0.08	0.08	0.09	0.10	0.11	0.12	0.13	0.15	0.16
	35	0.12	0.13	0.14	0.15	0.17	0.18	0.20	0.22	0.24
	40	0.18	0.19	0.21	0.23	0.25	0.27	0.29	0.31	0.33
70	20	0.05	0.06	0.06	0.07	0.07	0.08	0.09	0.10	0.11
	25	0.08	0.09	0.10	0.10	0.11	0.13	0.14	0.15	0.17
	30	0.12	0.13	0.14	0.16	0.17	0.19	0.21	0.22	0.24
	35	0.18	0.20	0.21	0.23	0.25	0.27	0.29	0.32	0.34
	40	0.26	0.28	0.30	0.33	0.35	0.37	0.40	0.43	0.45

Asian populations. The present study represents an attempt to assess the prevalence of, and risk factors for, undiagnosed diabetes in a rural Thai population. We found that approximately 4% of women and 7% of men in this population had undiagnosed type 2 diabetes. We also found that individuals at high risk of diabetes could be identified by a nomogram with 3 simple risk factors, namely, advancing age, high BMI, and high systolic blood pressure.

The prevalence of undiagnosed diabetes in this population is relatively lower than previous estimates in other Asian populations [3–5]. However, it should be noted that the present estimates were derived from a rural population, whereas previous studies have largely been based on urban populations. Rural populations are known to have lower risk of type 2 diabetes than urban populations [20,21]. Taken together, these data seem to suggest that there is a considerable difference in the prevalence of diabetes between urban and rural populations. As in other developing countries, Thailand has gone through rapid economic transition, with urbanization taking place in the entire country. In parallel with the economic change, the population health is in a transitional state with dramatic shift in lifestyle. These data suggest that diabetes and obesity and associated diseases are now considered a public health concern in Thailand, replacing the ''traditional'' concerns such as under-nutrition and infectious diseases.

The three factors that were identified in this study to be associated with type 2 diabetes have biologic basis. Although hypertension has long been known to be a consequence of type 2 diabetes, recent studies seem to suggest that may be an antecedent of diabetes. Our cross-sectional finding is consistent with the finding from a prospective study, in which Conen et al. [22] showed that baseline blood pressure was a strong predictor of type 2 diabetes. A prospective relationship between hypertension and diabetes may have a biologic basis. Increased central sympathetic drive is hypothesized to cause both hypertension, obesity, and in particular central obesity [23]. There are long-term studies linking early measures of increased sympathetic activity and blood pressure response to later obesity and diabetes [24,25]. Nevertheless, whether hypertension is a risk factor for, or a consequence of, diabetes is probably less relevant to the purpose of identifying high-risk individuals. A somewhat similar model has also been developed for the Vietnamese population [3], which uses waist-to-hip ratio and systolic blood pressure as predictors. In our study, we did not measure waist-to-hip ratio, but instead used body mass index as a measure of fatness. In the Vietnamese study, the prevalence of diabetes was 10–13%, which is considerably higher than our estimates. Therefore the predicted risk of diabetes by the Ta et al.'s model is higher than the present model. However, there is no significant difference in AUC values between the present model and Ta et al.'s model.

Obesity is strongly related to type 2 diabetes, especially central fat, has long been recognized as a risk factor for type 2 diabetes [26]. In this study, we found that obesity, as represented by increased BMI, is a risk factor for diabetes independent of age and systolic blood pressure. While it could be argued that BMI is a less-than-optimal measure of central obesity, which is known to be a better predictor of diabetes, BMI is a measure that can be taken in any busy primary care setting. Moreover, BMI is also highly correlated with waist to hip ratio [27]. Taken together, result of this study confirms that BMI can be used as a simple and robust risk factor to identify individuals at high risk of type 2 diabetes.

The present study's findings should be interpreted within the context of strengths and potential weaknesses. A major strength of this study is that the diagnosis of DM was based on repeated fasting plasma glucose measurement, which minimized any possibility of misdiagnosis. The sample size was large enough to ensure that the study could assess modest effect sizes otherwise not possible in smaller studies. However, since the study was undertaken in a clinic setting, the prevalence of diabetes could have been over-estimated the true prevalence in rural populations. Since the setting was an Asian rural province, these results may not be generalizable to urban populations or non-Asian populations among whom lifestyle and demographic structure could be different from the present population. It should also be noted that the present nomogram as well as Ta et al.'s model [3] were developed based on a cross-sectional study, and the predicted risk reflects a long-term risk, not a time-specific risk which would require a prospective study.

There are few prognostic models for predicting diabetes risk in Asians. Most previous models [3,10–13] used risk factors such age, sex, family history of diabetes, indicators of hypertension (e.g., systolic BP, use of anti-hypertensive drugs), and measures of obesity (e.g., BMI, waist circumference). The area under the ROC curve of these models varied between 0.54 and 0.83. In this study, the model with 3 factors (e.g., age, systolic blood pressure and BMI) yielded an AUC of 0.70 for women and 0.77 for men which are quite comparable with previous findings. There are, however, a number of differences between our model and previous models. Most previous models, such as the Gao et al.'s model [10], were based on the concept of risk stratification, in which continuous variables were categorized into subgroups, whereas our model was based on the concept of individualization, in which the continuous nature of risk factors were preserved in order to increase the degree of uniqueness of an individual. With continuous variables, the more risk factors are considered, the greater likelihood of uniqueness of an individual's profile can be defined. Therefore, by modeling risk factors in their continuous scale the present models can be uniquely tailored to an individual.

Assessment of absolute risk of diabetes can have practical application in treatment allocation, risk communication, and decision making. Since unselective screening for diabetes is not cost-effective, the nomogram presented here can be used as an initial screening tool and then followed by further confirmatory or diagnostic tests, including assessment of glycemia, HbA1c, lipids and family history. However, the predicted risk is a continuous probabilistic variable ranging from 0 to 1, and this raises the issue of selecting an optimal cut-off predicted probability to classify an individual into diabetic or non-diabetic group. This is not easy, because the cut-off value depends on the complex risk-benefit consideration, and perhaps more importantly, an individual's perception of risk, which is beyond the scope of the present study. The risk threshold by which an individual should be selected for further testing needs further research to maximize the cost-effectiveness of screening in rural populations. Moreover, the model presented here is preliminary in the sense that it is yet to be validated in a totally independent population. Therefore, both external and internal validation should be a priority of research in the application of risk assessment models.

In summary, these data show that approximately 4% of women and 7% of men in a rural population in Thailand had undiagnosed type 2 diabetes, and that increased BMI, raised blood pressure and advancing age were independent predictors of the risk type 2 diabetes. The prognostic model in the form of nomogram developed from this study should help primary care physicians to identify high-risk individuals for further diagnostic test.

Conflict of interest

There are no conflicts of interest.

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