

# A Prediction Model of the Incidence of Type 2 Diabetes in Individuals with Abdominal Obesity: Insights from the General Population

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**Background:** This study aimed to distinguish the risk factors for type 2 diabetes mellitus (T2DM) and construct a predictive model of T2DM in Japanese adults with abdominal obesity.

**Methods:** This study was a post hoc analysis. A total of 2012 individuals with abdominal obesity were included and randomly divided into training and validation groups at 70% (n = 1518) and 30% (n = 494), respectively. The LASSO method was used to screen for risk variables for T2DM, and to construct a nomogram incorporating the selected risk factors in the training group. We used the C-index, calibration plot, decision curve analysis, and cumulative hazard analysis to test the discrimination, calibration and clinical significance of the nomogram.

**Results:** In the training cohort, the C-index and receiver operating characteristic were 0.819 and the 95% CI was 0.776–0.858, with a specificity and sensitivity of 77% and 74.68%, respectively. In the validation cohort, the C-index was 0.853; sensitivity and specificity were 77.6% and 88.1%, respectively. The decision curve analysis showed that the model's prediction was effective and cumulative hazard analysis demonstrated that the high-risk score group was more likely to develop T2DM than the low-risk score group.

**Conclusion:** This nomogram may help clinicians screen abdominal obesity at a high risk for T2DM.

**Keywords:** type 2 diabetes, T2DM, abdominal obesity, nomogram, prediction model

## Background

Type 2 diabetes mellitus (T2DM) is a major public health concern, with incidence increasing due to improvements in living standards and sedentary lifestyle changes.<sup>1</sup> It has rapidly become a serious public health problem in both developed and developing countries in recent decades due to the rise in obesity and sedentary lifestyle.<sup>2,3</sup> It has caused a tremendous burden on the global healthcare system. Studies have reported that the economic burden in the US alone was estimated at \$327 billion in 2017.<sup>4</sup> T2DM can lead to multiple metabolic disorders and various acute and chronic complications due to insulin resistance and insufficient insulin production.<sup>3,5</sup>

Obesity is considered a contributing factor to T2DM, and reports have suggested that severe obesity in childhood and adolescence leads to a higher risk of T2DM in adults.<sup>2,6</sup> Currently, large numbers of studies have demonstrated that obesity, caused with low nutritional value and sedentary lifestyle, presents the greatest risk for incidence of T2DM in adults.<sup>6–8,10</sup> Insulin resistance is considered a main risk factor for T2DM in lean individuals with DM before they become obese and is correlated with T2DM due to excessive fat accumulation. However, not all obese patients develop T2DM. A previous study reported that more than 80% of people diagnosed with T2DM are obese, but 85% of obese individuals never develop diabetes.<sup>9</sup> Recently, the National Diabetes Statistics Report showed that 87.5% of people with diabetes

mellitus are obese, but the 18.4 million individuals who have diabetes and are overweight represent only 13.8% of all adults diagnosed with obesity in the United States in 2016.<sup>6,10</sup> Moreover, appropriate detection the risk factors of T2DM in obese patients is beneficial for early prevention and diagnosis of obese patients. The clinical evaluation of obesity is mainly based on the body mass index (BMI); however, obesity is mainly caused by abdominal obesity.<sup>11,12</sup> Studies investigating risk factors or models of T2DM in the abdominal obesity population are limited.

Risk prediction models are useful tools in the decision-making process of the patient. A previous study reported that such models can estimate the risk score of diabetes and improve patient prognosis in obese patients.<sup>2</sup> In addition to complex mathematical formulations and population heterogeneity, simple and intuitive tools can facilitate the implementation of these risk-prediction models. The nomogram transforms a complex regression equation into a simple and intuitive graph, which has great clinical application value.<sup>13</sup>

Thus, this study aimed to distinguish the risk variables of T2DM and construct a predictive model of T2DM in Japanese adults with abdominal obesity.

## Materials and Methods

### Research Design and Data Source

This was a post hoc analysis study using public health data. We used data from a population-based longitudinal database downloaded from the “DATADRYAD” database, as previously described.<sup>7</sup> NAGALA (NAfld in the Gifu Area, Longitudinal Analysis) data were uploaded to the DRYAD database by Okamura,<sup>7</sup> who granted that the data could be analyzed freely based on different scientific hypotheses. NAGALA is a cohort study based on the general population that has been ongoing since 1994.<sup>7</sup> To evaluate the risk factors of common chronic diseases in the general population and provide useful data for the early prevention and treatment of chronic diseases. NAGALA’s design has been described in detail before.

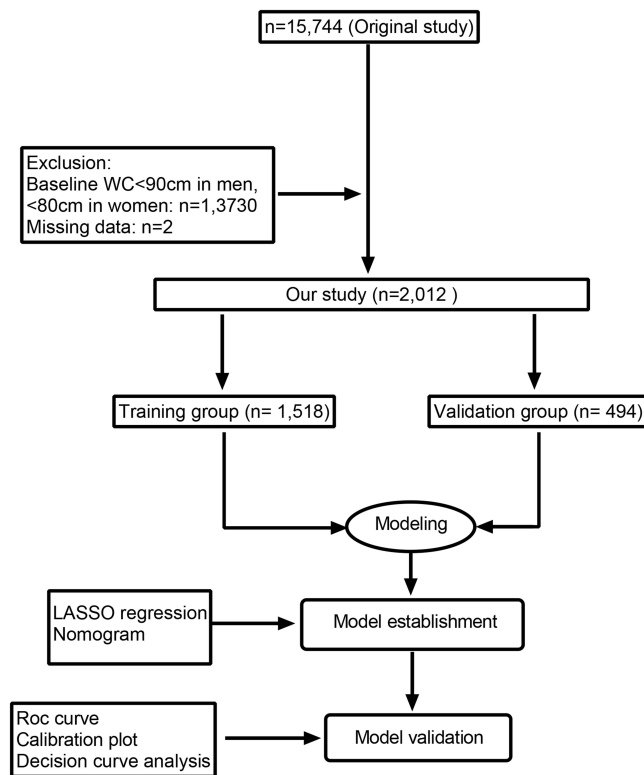
### Study Population

From 2004 to 2015, 15,744 individuals were enrolled in the original research and screened based on the inclusion and exclusion criteria.<sup>7</sup> According to prior studies, this study enrolled 2012 individuals after exclusion and explored the construction of non-invasive metrics-based predictive models of the 3-year and 6-years incidence of T2DM in participants with abdominal obesity (Figure 1). The exclusion criteria were as follows: (1) participants without abdominal obesity:<sup>14</sup> men, waist circumference <90 cm; women, waist circumference <80 cm. (2) Individuals with missing data. Because the research was a secondary analysis of the prior dataset and the original data were collected anonymously, requirement of informed consent was waived. This study was conducted in accordance with the Declaration of Helsinki. Okamura et al proved that the research was approved by the Murakami Memorial Hospital Ethics Committee (IRB number: 2018–09–01), and informed consent was obtained from each person. The study was also viewed and approved by the Ethics Review Committee of the Affiliated Changsha Central Hospital, University of South China. Since the subjects’ identifying information was removed from the data and uniformly replaced with a health check code, and informed consent was obtained from each subject to use the data from the previous study, no further application for informed consent was required for this study.

### Data Collection and Measurements

As described in the original data, alcohol habits, smoking, physical activity, and medical history were obtained using a standardized questionnaire. Alcohol consumption was divided into four groups:<sup>15</sup> more than 280 g per week was regarded as heavy alcohol consumption; 140–280 g per week was regarded as moderate; 40–140 g per week was regarded as light; and less than 40 g per week as no or minimal alcohol consumption.

Clinical information on a participant’s health check-up was composed of standardized and uniform questionnaire records used by trained medical staff, including systolic blood pressure (SBP), diastolic blood pressure (DBP), age, weight, sex, waist circumference (WC), smoking status, and exercise habits. Laboratory test indicators included triglyceride (TG), glycated hemoglobin A1c (HbA1c), high-density lipoprotein cholesterol (HDL-C), fasting blood



**Figure 1** Flow diagram of study design.

glucose (FPG), total cholesterol (TC), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT) were measured using an automatic biochemistry analyzer.

## Outcomes

All participants underwent regular physical check-ups at Murakami Memorial Hospital, and as mentioned earlier, 60% of the individuals underwent check-ups once or twice a year.<sup>7</sup> Event T2DM was defined as the occurrence of at least one of the following conditions during follow-up: self-reported diagnosis of T2DM, FPG level  $\geq 7$  mmol/L, or HbA1c level  $\geq 6.5\%$ .<sup>16</sup>

## Statistical Analysis

The study is consistent with the transparent report of the multivariate predictive model of individual prognosis or diagnosis (TRIPOD),<sup>17</sup> which is showed in [Supplementary Material](#).

R software (version R-4.1.2, <http://www.r-project.org>) was used for analysis and data processing. All enrolled patients were randomly divided into training and validation groups at 70% and 30% by simple randomization using R software function of `set.seed()`, respectively. Continuous variables are shown as medians (quartiles) or means  $\pm$  standard deviations, while categorical variables are shown as percentages or frequencies. *t*-tests were used to analyze differences between the training and validation cohorts for normally distributed continuous variables, chi-square tests for categorical variables, and Wilcoxon rank-sum tests for nonnormally distributed continuous variables. The least absolute shrinkage and selection operator (LASSO) regression analysis was performed to identify risk variables by shrinkage and variable selection for linear regression models. To achieve the subset of predictive variables, LASSO regression methods excluded irrelevant variables, which are estimated values near zero. The variables from the LASSO regression analysis by 10-fold cross-validation were visualized to construct the nomogram. The nomogram showed the variables selected by the LASSO model and the corresponding contributions in predicting T2DM in patients with abdominal obesity. The

prediction was added from each value for individuals based on a point scale. Finally, the 3-years and 6-years risk of T2DM were obtained using the total points scale.

Receiver operating characteristic (ROC) curve analysis was performed to estimate the prediction ability of the training group model. Calibration curves were drawn for the training and validation groups, and the Hosmer–Lemeshow fitting test was used to evaluate the calibration validity of the prediction model. Decision curve analysis (DCA) was used to evaluate the clinical utility of nomogram prediction for the training and validation groups. The ROC curve, C index, calibration curve, and DCA were analyzed by bootstrap resampling to reduce overfitting bias. Statistical significance was set at  $P < 0.05$ .

## Results

### Characteristics of the Study Participants

The study included all 2012 participants with abdominal obesity after applying the exclusion and inclusion criteria (Figure 1). The mean age of the participants was 45.42 years, 52.14% of the eligible subjects were men, and the incidence of type 2 diabetes mellitus was 6.81%. A total of 1518 participants were randomly divided into the training group and 494 into the validation group. The variables in Table 1 had no statistically significant differences between the two cohorts.

**Table 1** Demographic and Clinical Characteristics of Study Population

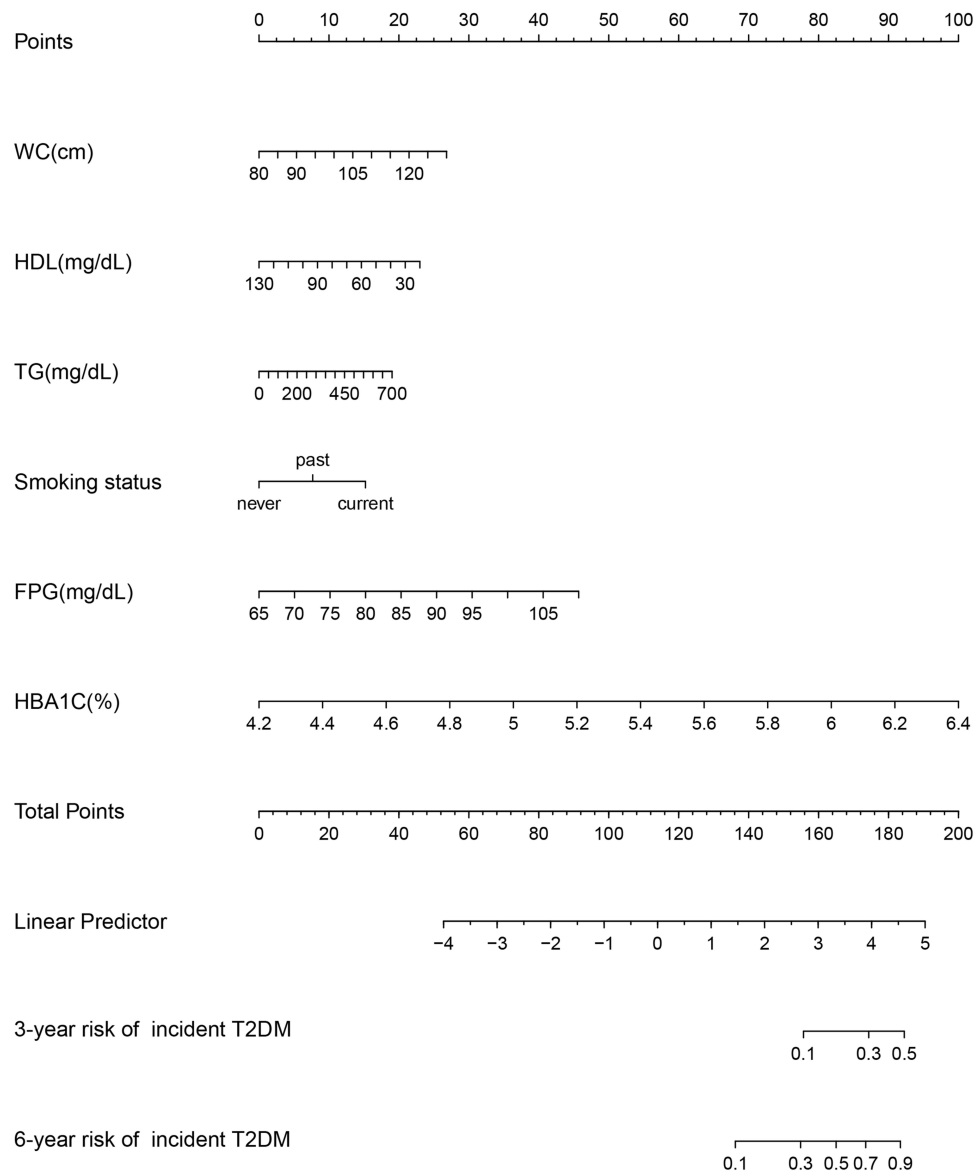
Characteristic	All	Derivation Cohort	Validation Cohort	P-value
No. of participants	2012	1518	494	
Age (years)	45.42 ± 8.72	45.41 ± 8.70	45.44 ± 8.77	0.952
BMI (kg/m <sup>2</sup> )	26.63 ± 3.17	26.66 ± 3.16	26.55 ± 3.21	0.501
WC (cm)	89.95 ± 7.06	89.89 ± 7.05	90.13 ± 7.11	0.511
Weight (kg)	73.42 ± 13.18	73.49 ± 13.27	73.19 ± 12.92	0.670
ALT (IU/L)	27.00 ± 19.63	27.05 ± 19.68	26.81 ± 19.53	0.815
AST (IU/L)	20.99 ± 10.08	21.01 ± 10.45	20.92 ± 8.89	0.861
GGT (IU/L)	25.38 ± 21.63	25.38 ± 21.82	25.40 ± 21.10	0.989
HDL (mg/dl)	50.33 ± 13.28	50.30 ± 13.27	50.44 ± 13.33	0.839
TC (mg/dl)	208.97 ± 33.67	208.56 ± 33.72	210.35 ± 33.49	0.305
TG (mg/dl)	106.92 ± 68.36	105.55 ± 65.87	111.07 ± 75.51	0.119
HBA1C (%)	5.30 ± 0.33	5.30 ± 0.33	5.30 ± 0.33	0.936
FPG (mg/dl)	95.66 ± 7.04	95.61 ± 7.03	95.76 ± 7.06	0.665
Follow-up duration (months)	60.65 (26.68, 105.78)	60.59 (28.73, 106.22)	60.43 (24.64, 102.67)	0.388
Gender [n (%)]				0.418
Male	1050 (52.19%)	800 (52.70%)	250 (50.61%)	
Female	962 (47.81%)	718 (47.30%)	244 (49.39%)	
Habit of exercise, [n (%)]				0.889
No	1755 (87.23%)	1325 (87.29%)	430 (87.04%)	
Yes	257 (12.77%)	193 (12.71%)	64 (12.96%)	
Drinking status, [n (%)]				0.395
Non or small	1579 (78.47%)	1186 (78.13%)	393 (79.55%)	
Light	210 (10.44%)	159 (10.47%)	51 (10.32%)	
Moderate	154 (7.65%)	124 (8.17%)	30 (6.07%)	
Heavy	69 (3.44%)	49 (3.23%)	20 (4.05%)	
Smoking status, [n (%)]				0.884
Never	1224 (60.83%)	923 (60.80%)	301 (60.93%)	
Past	351 (17.45%)	268 (17.65%)	83 (16.80%)	
Current	437 (21.72%)	327 (21.54%)	110 (22.27%)	
Incident T2DM, [per 1000, 95% CI]	6.81 (5.74, 7.99)	6.58 (5.39, 7.95)	7.49 (5.32, 10.17)	0.489

## LASSO Regression Analysis in Training Cohort and Dev

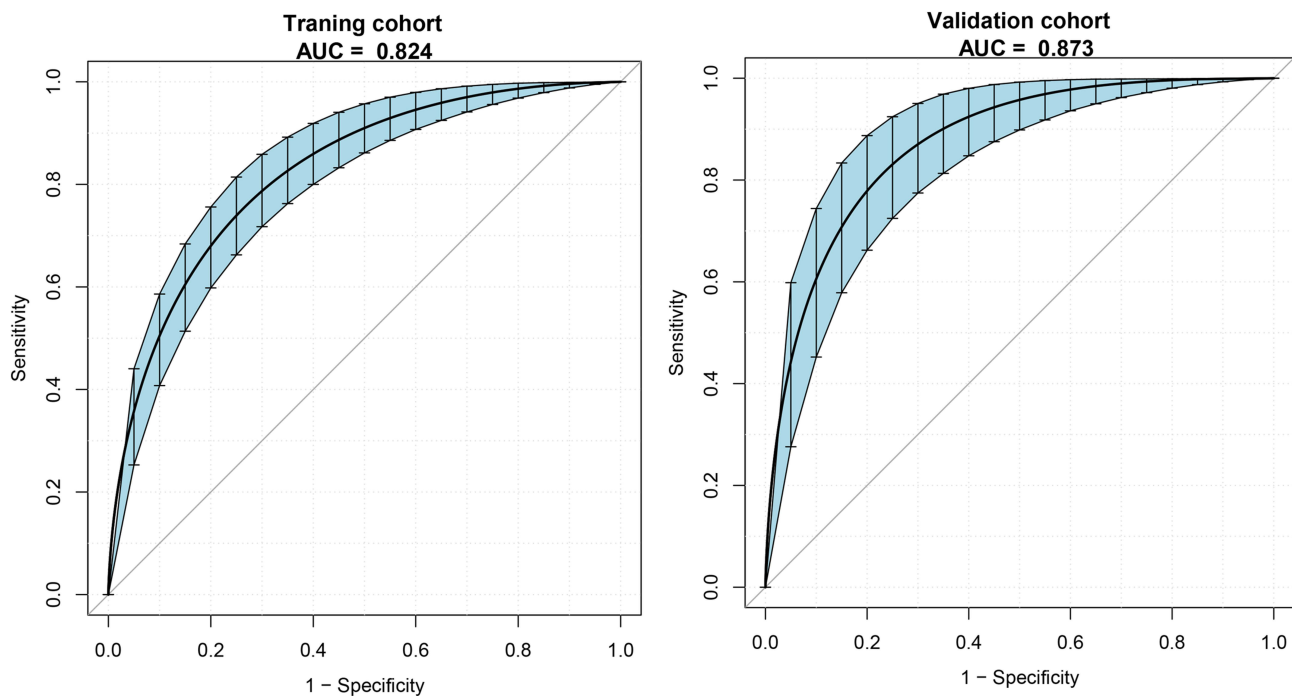
Sixteen potential risk factors were selected based on basic characteristics, and LASSO regression was performed using 10-fold cross-validation (Figure S1). Factors that were not near zero were selected using LASSO regression. A total of 10 factors were excluded, and six factors were selected, including WC, HbA1c, FPG, HDL, TG, and smoking status. Lambda.lse was 0.015, and the coefficients of the variables are listed in Table S1. We further combined the six potential risk factors into a prediction model and displayed them using a nomogram (Figure 2).

## Performance of the Derivation and Validation Cohort

The C-index was used to estimate the performance of the prediction model. For the derivation cohort, the area under the ROC curve was 0.82, 95% CI was 0.78 to 0.86, and sensitivity and specificity were 73.0% and 79.4%, respectively. In the validation cohort, the C-index was 0.872, 95% CI was 0.82 to 0.92, and the results of bootstrap resampling validation (times=1000) confirmed that the nomogram's performance was stable in the validation sets (Figure 3). Sensitivity and



**Figure 2** Nomogram for predicting the 3-year and 6-years risk of T2D in adults with abdominal obesity. To use the nomogram, an individual patient's value is located on each variable axis, and a line is drawn upward to determine the number of points received for each variable value. The scores for all variables are then added to obtain the total score, and a vertical line is drawn from the total-points row to estimate the 3-year and 6-years risk of T2D in adults with abdominal obesity at the lower line of the nomogram.



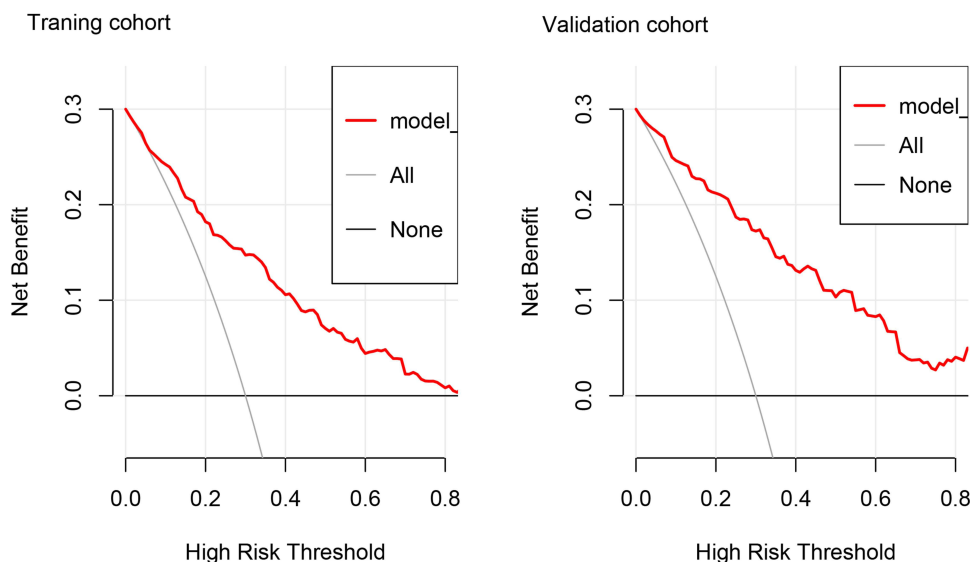
**Figure 3** ROC curve of the nomogram in the training and validation cohort (bootstrap resampling times = 1000).

**Abbreviations:** ROC, receiver operating characteristic; AUC, area under the curve.

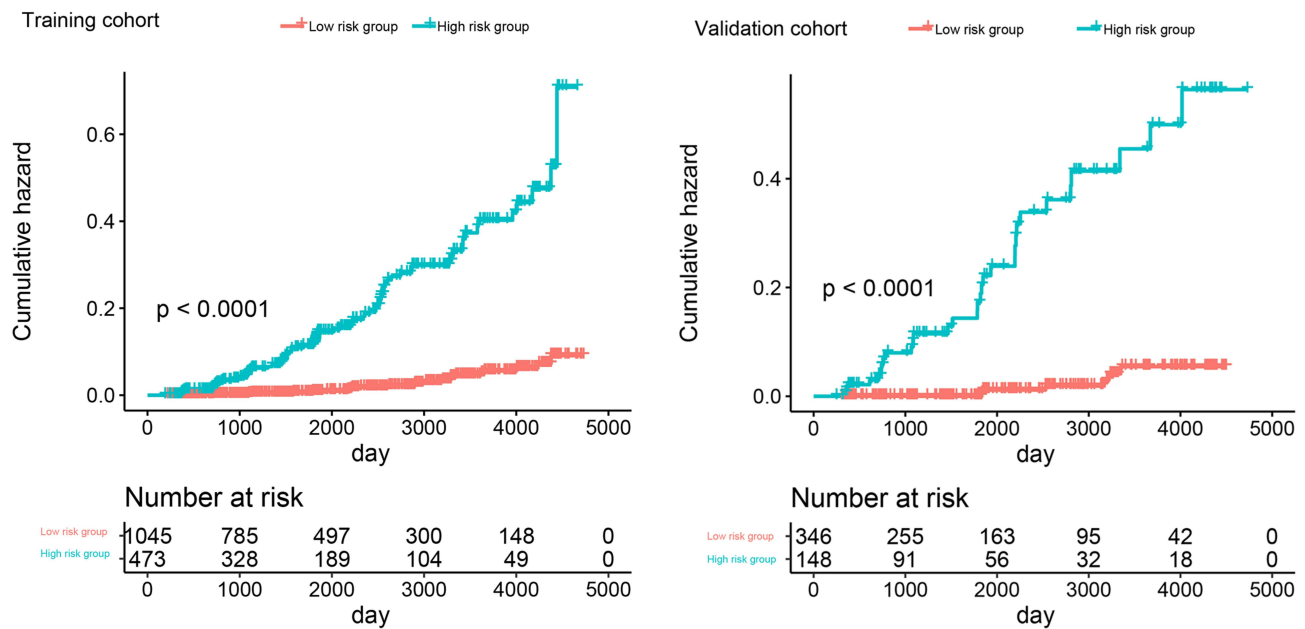
specificity in the validation cohort were 78.3% and 81.61%, respectively. Calibration curves were obtained by constructing the calibration of the nomogram prediction model using the Hosmer–Lemeshow fitting test (Figure S2). Using the Hosmer–Lemeshow test, the statistics between the predicted risk of T2DM and observed risk were not significantly different after bootstrap resampling validation (times=1000).

## Decision Curve of the Predicting Nomogram and Validation Cohort

Decision curve analysis of the training and validation groups showed that the predictive model was more effective in predicting the risk of T2DM incidence at 3 and 6 years in Japanese patients with abdominal obesity (Figure 4).



**Figure 4** Decision curve analysis of the nomogram in the training and validation cohorts. The y-axis stands the net benefit. The x-axis indicates the threshold probability. The red line represents the nomogram. The black line displays the net benefit of the strategy of treating no patients. The gray line displays the net benefit of the strategy of treating all patients (bootstrap resampling times = 1000).



**Figure 5** Cumulative hazard analysis of risk group stratification based on the predictor from nomogram prediction. Cumulative hazard analysis showed the T2DM incidence probability of high risk and low risk group between the training cohort and the validation cohort.

## Cumulative Hazard Analysis of the Prediction Model

In addition, as previously reported, each patient was assigned to the high-risk or low-risk group based on the 50% cut-off predicted by the prediction model. Cumulative hazard analysis revealed significant differences in T2DM incidence rates between the training and validation groups (Figure 5). This stratification could effectively distinguish the incidence of T2DM between the two risk groups in the training and validation groups.

## Development of Webserver for Easy Access of Our New Model

To help researchers and clinicians better use the nomogram, our online version can be accessed at <https://xy2yyjzyxk.shinyapps.io/T2DmOBESITY/>. By inputting clinical characteristics and reading the output data and tables generated by the web server, the predicted incidence of T2DM in individuals with abdominal obesity can be easily determined.

## Discussion

Obesity is an important risk factor for the onset of T2DM.<sup>2,18,19</sup> BMI is considered a marker for obesity and a predictor variable for most risk models of diabetes. However, studies have suggested that BMI does not reflect central obesity. WC is a better predictor of the incidence of T2DM than BMI,<sup>20,21</sup> which is consistent with the results of our research. Studies found that lifestyle, environmental factors, and nutritional status are associated with obesity and T2DM.<sup>6</sup> However, many obese individuals never develop diabetes.<sup>9</sup> There are a number of existing studies that construct nomogram to predict T2DM events in individuals.<sup>2,19,22</sup> However, none of these studies focused on obese individuals with abdominal obesity. There is an urgent need to identify risk factors for T2DM in obese individuals.

Based on the data from the NAGALA cohort study, we developed a nomogram and validated the model to predict the incidence of T2DM in obese individuals with abdominal obesity and to help clinicians screen individuals at a high risk for T2DM. In addition, the nomogram showed excellent discrimination. Accurate cumulative hazard predictions of the proposed nomograms are indicated by calibration curves. The decision curve analysis showed that the model's prediction was more effective. Furthermore, cumulative hazard analysis demonstrated that the high-risk score group was more likely to develop T2DM than the low-risk score group.

Previous studies have developed nomograms that predict the 5-year risk of T2DM in non-obese adults based on age, gamma-glutamyl transferase, fatty liver, HbA1c, TG, and FPG.<sup>2</sup> In this study, six parameters were selected for the



prediction model: WC, HDL, TG, smoking status, FPG, and HbA1c. Notably, non-obese adults are at an increased risk of T2DM, similar to that of obese individuals. The risk variables for T2DM were consistent with prior studies.<sup>2,19,23–25</sup> Studies have suggested that the accumulation sites of body fat are associated with blood glucose levels.<sup>25–27</sup> Moreover, WC is a better measure of abdominal obesity than BMI.<sup>28,29</sup> Obesity markers (Waist circumference, waist-to-height ratio, and waist-hip ratio) are associated with reactive oxygen species levels. Excess production of reactive oxygen species leads to insulin resistance.<sup>30</sup> In addition, increased levels of inflammatory markers in adipocytes are associated with impaired insulin signaling pathways.<sup>31</sup> Inflammatory cytokines and adipocytokines are associated with central obesity.<sup>32</sup> All of these factors are closely related to an increased risk of T2DM.

Previous studies have reported that dyslipidemia is one of the highest risk factors for impaired fasting glucose levels and T2DM.<sup>4,33</sup> Similarly, elevated TG and low level of HDL were associated with a higher T2DM risk in our nomogram. HDL may inhibit the incidence of T2DM by decreasing apoptotic loss of pancreatic  $\beta$ -cells and endoplasmic reticulum (ER) stress.<sup>34</sup> Adipose tissue, as an endocrine organ, can affect lipid metabolism and glucose levels, and TG is the most abundant lipid in adipose tissue. TG may directly contribute to glucose metabolism disorders. Thus, dyslipidemia may have underlying pathophysiological changes in individuals with abdominal obesity that contribute to T2DM and heterogeneity may exist among individuals.

In our nomogram, participants who were past or current smokers were more likely to develop T2DM than those who never smoked. In Japan, a systematic review and meta-analysis suggested that cigarette smoking is not only related to an increased incidence of T2DM but also could have a substantial effect on increasing the burden of T2DM.<sup>35</sup> Additionally, a meta-analysis and system review of 88 prospective studies with nearly six million participants and 295,446 incident cases reported that tobacco smoking increased the incidence of T2DM in comparison to nonsmokers.<sup>36</sup> The World Health Organization (WHO) also recommends smoking cessation to prevent T2DM. To date, a complete understanding of the mechanisms underlying tobacco abuse and pancreatic  $\beta$  cell damage is lacking. However, numerous studies have indicated that smoking and nicotine can affect pancreatic beta cell function, body composition, and peripheral insulin sensitivity.<sup>37,38</sup>

HbA1c is a well-known and efficient predictor and diagnostic tool of T2DM<sup>39</sup> and its various complications. An ambidirectional cohort study indicated that patients with both high FPG and abnormal HbA1c are at a higher risk of developing T2DM, while HbA1c in combination with FPG may help distinguish the subgroups with the highest risk of diabetes in people with impaired fasting glucose.<sup>9,40</sup> Elevated FPG levels are associated with lower insulin response and sensitivity and are related to an increased incidence of T2DM.<sup>41</sup>

To the best of our knowledge, this is the first nomogram to predict incident T2DM in obese patients with abdominal obesity, using a standardized lifestyle factor questionnaire. The scale of research data is relatively large in Japan. Currently, obesity is the most important risk factor leading to the onset of T2DM. Our nomogram can improve primary care strategies and facilitate appropriate T2DM detection in obese individuals, which has good value for public health care benefit. In order to better apply in clinical practice, we consider that the variables needed in nomogram are common and easy to obtain in clinical practice. This study has some limitations. First, our validation group consisted of the same individuals as the training group, which may suggest that the results were too optimistic. Second, this large-scale cohort study focused on a Japanese population. Whether the model exhibits better power in other ethnicities requires further validation in external cohorts. Third, due to the second analysis, some indicators, or novel biochemical markers, such as genetic factors, could not be adjusted in this study.

## Conclusion

In summary, we developed a nomogram and validated the model to predict the incidence of T2DM in obese individuals with abdominal obesity to help clinicians screen individuals at a high risk for T2DM. The nomogram is of great utility because of the accessibility of its online version and its easily available parameters.

## Abbreviations

BMI, body mass index; T2DM, type 2 diabetes mellitus; SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; TG, triglyceride; HbA1c, glycated hemoglobin A1c; FPG, fasting blood glucose; TC, total



cholesterol; HDL-C, high-density lipoprotein cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; WHO, World Health Organization; ER, endoplasmic reticulum; DCA, decision curve analysis; LASSO, the least absolute shrinkage age and selection operator; ROC, receiver operating characteristic.

## Data Sharing Statement

The datasets that support the conclusions of this article can be found in the Dryad repository.

## Ethics Approval and Consent to Participate

As the authorization of the ethics committee of Murakami Memorial Hospital has been obtained in the previous study, this study does not need to be submitted for ethical approval again.

## Acknowledgments

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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## References

1. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nat Rev Endocrinol.* 2018;14(2):88–98. doi:10.1038/nrendo.2017.151
2. Cai XT, Ji LW, Liu SS, et al. Derivation and validation of a prediction model for predicting the 5-year incidence of type 2 diabetes in non-obese adults: a population-based cohort study. *Diabetes Metab Syndr Obes.* 2021;14:2087–2101. doi:10.2147/DMSO.S304994
3. Kautzky-Willer A, Harreiter J, Pacini G. Sex and gender differences in risk, pathophysiology and complications of type 2 diabetes mellitus. *Endocr Rev.* 2016;37(3):278–316. doi:10.1210/er.2015-1137
4. American Diabetes A. Economic costs of diabetes in the U.S. in 2017. *Diabetes Care.* 2018;41(5):917–928. doi:10.2337/dci18-0007
5. Nair GG, Tzanakakis ES, Hebrok M. Emerging routes to the generation of functional beta-cells for diabetes mellitus cell therapy. *Nat Rev Endocrinol.* 2020;16(9):506–518. doi:10.1038/s41574-020-0375-3
6. Malone JJ, Hansen BC. Does obesity cause type 2 diabetes mellitus (T2DM)? Or is it the opposite? *Pediatr Diabetes.* 2019;20(1):5–9. doi:10.1111/pedi.12787
7. Okamura T, Hashimoto Y, Hamaguchi M, et al. Ectopic fat obesity presents the greatest risk for incident type 2 diabetes: a population-based longitudinal study. *Int J Obes.* 2019;43(1):139–148. doi:10.1038/s41366-018-0076-3
8. Zhao W, Tong JJ, Cao YT, et al. A linear relationship between a body shape index and risk of incident type 2 diabetes: a secondary analysis based on a retrospective cohort study in Japan. *Diabetes Metab Syndr Obes.* 2020;13:2139–2146. doi:10.2147/DMSO.S256031
9. Tanamas SK, Reddy SP, Chambers MA, et al. Effect of severe obesity in childhood and adolescence on risk of type 2 diabetes in youth and early adulthood in an American Indian population. *Pediatr Diabetes.* 2018;19(4):622–629. doi:10.1111/pedi.12627
10. Hales CM, Carroll MD, Fryar CD, et al. Prevalence of obesity among adults and youth: United States, 2015–2016. *NCHS Data Brief.* 2017;2017(288):1–8.
11. Shulman GI. Ectopic fat in insulin resistance, dyslipidemia, and cardiometabolic disease. *N Engl J Med.* 2014;371(23):2237–2238. doi:10.1056/NEJMc1412427
12. Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. *Endocr Rev.* 2000;21(6):697–738. doi:10.1210/edrv.21.6.0415
13. Balachandran VP, Gonen M, Smith JJ, et al. Nomograms in oncology: more than meets the eye. *Lancet Oncol.* 2015;16(4):e173–80. doi:10.1016/S1470-2045(14)71116-7
14. Misra A, Vikram NK, Gupta R, et al. Waist circumference cutoff points and action levels for Asian Indians for identification of abdominal obesity. *Int J Obes.* 2006;30(1):106–111. doi:10.1038/sj.ijo.0803111

15. Hashimoto Y, Hamaguchi M, Kojima T, et al. Modest alcohol consumption reduces the incidence of fatty liver in men: a population-based large-scale cohort study. *J Gastroenterol Hepatol.* 2015;30(3):546–552. doi:10.1111/jgh.12786
16. American Diabetes A. Standards of medical care in diabetes--2011. *Diabetes Care.* 2011;34(Suppl 1):S11–61. doi:10.2337/dc11-S011
17. Collins GS, Reitsma JB, Altman DG, et al. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. *BMJ.* 2015;350:g7594. doi:10.1136/bmj.g7594
18. Bhupathiraju SN, Hu FB. Epidemiology of obesity and diabetes and their cardiovascular complications. *Circ Res.* 2016;118(11):1723–1735. doi:10.1161/CIRCRESAHA.115.306825
19. Cai X, Zhu Q, Cao Y, et al. A prediction model based on noninvasive indicators to predict the 8-year incidence of type 2 diabetes in patients with nonalcoholic fatty liver disease: a population-based retrospective cohort study. *Biomed Res Int.* 2021;2021:5527460. doi:10.1155/2021/5527460
20. Wei J, Liu X, Xue H, Wang Y, Shi Z. Comparisons of visceral adiposity index, body shape index, body mass index and waist circumference and their associations with diabetes mellitus in adults. *Nutrients.* 2019;11(7):1580. doi:10.3390/nu11071580
21. Venkatrao M, Nagarathna R, Patil SS, et al. A composite of BMI and waist circumference may be a better obesity metric in Indians with high risk for type 2 diabetes: an analysis of NMB-2017, a nationwide cross-sectional study. *Diabetes Res Clin Pract.* 2020;161:108037. doi:10.1016/j.diabres.2020.108037
22. Wilkinson L, Yi N, Mehta T, et al. Development and validation of a model for predicting incident type 2 diabetes using quantitative clinical data and a Bayesian logistic model: a nationwide cohort and modeling study. *PLoS Med.* 2020;17(8):e1003232. doi:10.1371/journal.pmed.1003232
23. Cai X, Zhu Q, Wu T, et al. Development and validation of a novel model for predicting the 5-year risk of type 2 diabetes in patients with hypertension: a retrospective cohort study. *Biomed Res Int.* 2020;2020:9108216. doi:10.1155/2020/9108216
24. Lin Z, Guo D, Chen J, et al. A nomogram for predicting 5-year incidence of type 2 diabetes in a Chinese population. *Endocrine.* 2020;67(3):561–568. doi:10.1007/s12020-019-02154-x
25. Wang K, Gong M, Xie S, et al. Nomogram prediction for the 3-year risk of type 2 diabetes in healthy mainland China residents. *EPMA J.* 2019;10(3):227–237. doi:10.1007/s13167-019-00181-2
26. Hirani V. Generalised and abdominal adiposity are important risk factors for chronic disease in older people: results from a nationally representative survey. *J Nutr Health Aging.* 2011;15(6):469–478. doi:10.1007/s12603-011-0051-3
27. Krishnan S, Rosenber L, Djousse L, et al. Overall and central obesity and risk of type 2 diabetes in U.S. black women. *Obesity.* 2007;15(7):1860–1866. doi:10.1038/oby.2007.220
28. Zhou Y, Yang G, Peng W, et al. Relationship between depression symptoms and different types of measures of obesity (BMI, SAD) in US women. *Behav Neurol.* 2020;2020:9624106. doi:10.1155/2020/9624106
29. Yang T, Zhao B, Pei D. Evaluation of the association between obesity markers and type 2 diabetes: a cohort study based on a physical examination population. *J Diabetes Res.* 2021;2021:6503339. doi:10.1155/2021/6503339
30. Klisic A, Kavacic N, Vujcic S, et al. Factorial analysis of the cardiometabolic risk influence on redox status components in adult population. *Oxid Med Cell Longev.* 2021;2021:6661940. doi:10.1155/2021/6661940
31. Ates E, Set T, Karahan SC, et al. Thiol/Disulphide homeostasis, ischemia modified albumin, and ferroxidase as oxidative stress markers in women with obesity with insulin resistance. *J Med Biochem.* 2019;38(4):445–451. doi:10.2478/jomb-2019-0015
32. Bragg F, Tang K, Guo Y, et al. Associations of general and central adiposity with incident diabetes in chinese men and women. *Diabetes Care.* 2018;41(3):494–502. doi:10.2337/dc17-1852
33. Athyros VG, Doumas M, Imprialos KP, et al. Diabetes and lipid metabolism. *Hormones.* 2018;17(1):61–67. doi:10.1007/s42000-018-0014-8
34. Chapman MJ. HDL functionality in type 1 and type 2 diabetes: new insights. *Curr Opin Endocrinol Diabetes Obes.* 2022;29(2):112–123. doi:10.1097/MED.0000000000000705
35. Akter S, Goto A, Mizoue T. Smoking and the risk of type 2 diabetes in Japan: a systematic review and meta-analysis. *J Epidemiol.* 2017;27(12):553–561. doi:10.1016/j.je.2016.12.017
36. Pan A, Wang Y, Talaei M, et al. Relation of active, passive, and quitting smoking with incident type 2 diabetes: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol.* 2015;3(12):958–967. doi:10.1016/S2213-8587(15)00316-2
37. Anker MS, Kalantar-Zadeh K, Doehner W. Smoking and other risk factors in type 2 diabetes. *N Engl J Med.* 2018;379(26):2572–2573. doi:10.1056/NEJMc1812842
38. Sliwiska-Mosson M, Milnerowicz H. The impact of smoking on the development of diabetes and its complications. *Diab Vasc Dis Res.* 2017;14(4):265–276. doi:10.1177/1479164117701876
39. American Diabetes A. 6. Glycemic targets: standards of medical care in diabetes-2021. *Diabetes Care.* 2021;44(Suppl1):S73–S84. doi:10.2337/dc21-S006
40. Thamakaisorn S, Anothaisintawee T, Sukhato K, et al. Hemoglobin A1c in combination with fasting plasma glucose trumps fasting plasma glucose alone as predictive indicators for diabetes mellitus: an ambidirectional cohort study of Thai people with impaired fasting glucose. *BMJ Open Diabetes Res Care.* 2021;9(2):e002427. doi:10.1136/bmjdr-2021-002427
41. Ogata E, Asahi K, Yamaguchi S, et al. Low fasting plasma glucose level as a predictor of new-onset diabetes mellitus on a large cohort from a Japanese general population. *Sci Rep.* 2018;8(1):13927. doi:10.1038/s41598-018-31744-4

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