

Estimation of atherosclerotic cardiovascular disease risk in type 2 diabetes

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To the Editor: The global prevalence of diabetes is increasing dramatically.^[1] To prevent and treat diabetes and its cardiovascular complications, clinical practice guidelines recommend to assess the prevalent non-modifiable risk factors in people with diabetes. The prediction for atherosclerotic cardiovascular disease (ASCVD) risk in China (China-PAR) model was specifically developed to predict the 10-year risk for ASCVD in China.^[2] The risk equations used in this model are based on data from two large contemporary cohorts of Chinese participants and included age, systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol (HDL-C), current smoking, and diabetes. Evaluation of this model showed good performance for 10-year ASCVD risk prediction among the Chinese population.

The evaluation of the effectiveness of the treatment paradigm for newly diagnosed type 2 diabetes (NEW2D) patients in China cohort was developed to investigate initial and ongoing treatments, as well as clinical outcomes, for participants with type 2 diabetes in China. This prospective, longitudinal cohort of 5770 participants indicated that the proportion who achieved glycemic targets significantly increased over time.^[3]

Prediction of future ASCVD risk is crucial for the planning and resourcing of prevention and intervention efforts, as well as the identification of those most at risk. Therefore, the primary aim of this study was to estimate the distribution of 10-year ASCVD risk among people with type 2 diabetes without prior glucose-lowering treatment as a proxy of “newly diagnosed” in the NEW2D study cohort using the China-PAR model.^[2] The secondary objectives were to evaluate the distribution of cardiovascular risk factors at baseline and the drug utilization pattern (antihypertensive treatment, lipid-lowering agents, ASCVD management algorithm) at baseline in the NEW2D study cohort.

NEW2D study (Clinicaltrials.gov identifier: NCT01525693) was a prospective multicenter cohort study designed to evaluate the progression and treatment pattern for newly diagnosed people with type 2 diabetes in China.^[3] In NEW2D study, 5770 participants from China aged at least 20 years with a confirmed diagnosis of type 2 diabetes made within the past 6 months were enrolled in, from June 2012 to February 2014 from 79 hospital outpatient departments in six major geographic regions of China. Participants received routine treatment (diet and exercise or medication) and were asked to return to the same investigator for follow-up visits at 3, 6, 9, and 12 months after their baseline visit. Medical history, comorbidities, health behavior, physical exam, laboratory tests, medications, and diabetes complications including ASCVD were obtained at baseline and at each follow-up visit.

NEW2D study was conducted in accordance with the ethical principles that have their origin in the *Declaration of Helsinki* and that are consistent with good pharmacoepidemiology practices and applicable laws and regulations. Ethical approval was initially obtained from the Peking University People's Hospital Ethics Committee, and subsequently from all of the hospitals participating in the study. All participants signed the informed consent form before inclusion in the study.

This analysis focused on ASCVD risk in participants who had not taken glucose-lowering treatments prior to their baseline visit in the NEW2D study. Participants missing data for major ASCVD risk factors or with a history of ASCVD at baseline were excluded. This analysis was performed using baseline data from the NEW2D study cohort. Data collection methods have been previously reported.^[3] Full details of the China-PAR model have been published previously.^[2] The 10-year ASCVD risk was defined as the risk of developing the first ASCVD event (myocardial infarction, stroke, and cardiovascular disease [CVD] death) over a 10-year period among a population without ASCVD at baseline. The ASCVD risk factors

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included in the China-PAR model were age, geographic region, urbanization, smoking status, waist circumference, treated and untreated systolic blood pressure, total cholesterol, HDL-C, and a family history of ASCVD events. The model included interaction terms of age with risk factors (treated or untreated systolic blood pressure, current smoking, and family history of ASCVD).^[2]

All continuous variables were summarized using descriptive statistics and analyzed using either one-way analysis of variance tests, Wilcoxon–Mann–Whitney tests, or Kruskal–Wallis tests. All categorical variables were summarized using descriptive statistics and analyzed using either Chi-square tests or Fisher’s exact tests. All statistical tests were two-sided, with significance set at 0.05. The 95% confidence intervals were determined wherever applicable. Statistical analyses were conducted using SAS (Cary, NC, USA), version 9.3 or above.

As a result, a total of 2301 participants were included in this analysis. A total of 3257 participants were excluded for taking oral blood glucose-lowering agents and/or insulin prior to baseline, 416 participants were excluded due to missing ASCVD risk factor data, and 59 participants were excluded due to having a history of ASCVD at baseline.

The participant characteristics by their predicted ASCVD risk levels are shown in Supplementary Table 1, <http://links.lww.com/CM9/A973>. The proportion of male was 55.3%, 24.2% were current smokers, the mean body mass index (BMI) was 25.1 kg/m², the mean systolic blood pressure was 128.6 mmHg, the mean HDL-C was 1.22

mmol/L, and the mean low-density lipoprotein cholesterol (LDL-C) was 3.00 mmol/L.

A total of 54.4% of participants was predicted, according to Chinese guidelines for the management of dyslipidemia in adults, to have a medium (5%–10%) or high risk (>10%) of developing ASCVD within 10 years.^[4] Baseline characteristics that were statistically different between the ASCVD risk categories included age, urban living, waist circumference, systolic blood pressure, antihypertensive treatment, hemoglobin A1c, HDL-C, anti-dyslipidemia treatment, cataract, and serum creatinine. There were no statistically significant differences observed between baseline LDL-C levels or BMI for the different ASCVD risk levels [Supplementary Table 1, <http://links.lww.com/CM9/A973>].

The estimated mean risk of ASCVD events was 7.4% among participants with type 2 diabetes who had not previously received glucose-lowering medication. The mean 10-year predicted ASCVD risk in participants without glucose-lowering treatments prior to the baseline visit and in participants without glucose-lowering, antihypertensive, or anti-dyslipidemia treatments prior to the baseline visit are shown in Supplementary Table 2, <http://links.lww.com/CM9/A973>. Age and systolic blood pressure were the most important determinants of ASCVD risk for men and women. The 10-year ASCVD risk distribution by systolic blood pressure, age, and sex is shown in Figure 1. A greater proportion of participants in higher CVD risk categories were taking antihypertensive and lipid-lowering medications compared with those in lower CVD risk categories [Supplementary Table 2, <http://links.lww.com/CM9/A973>].

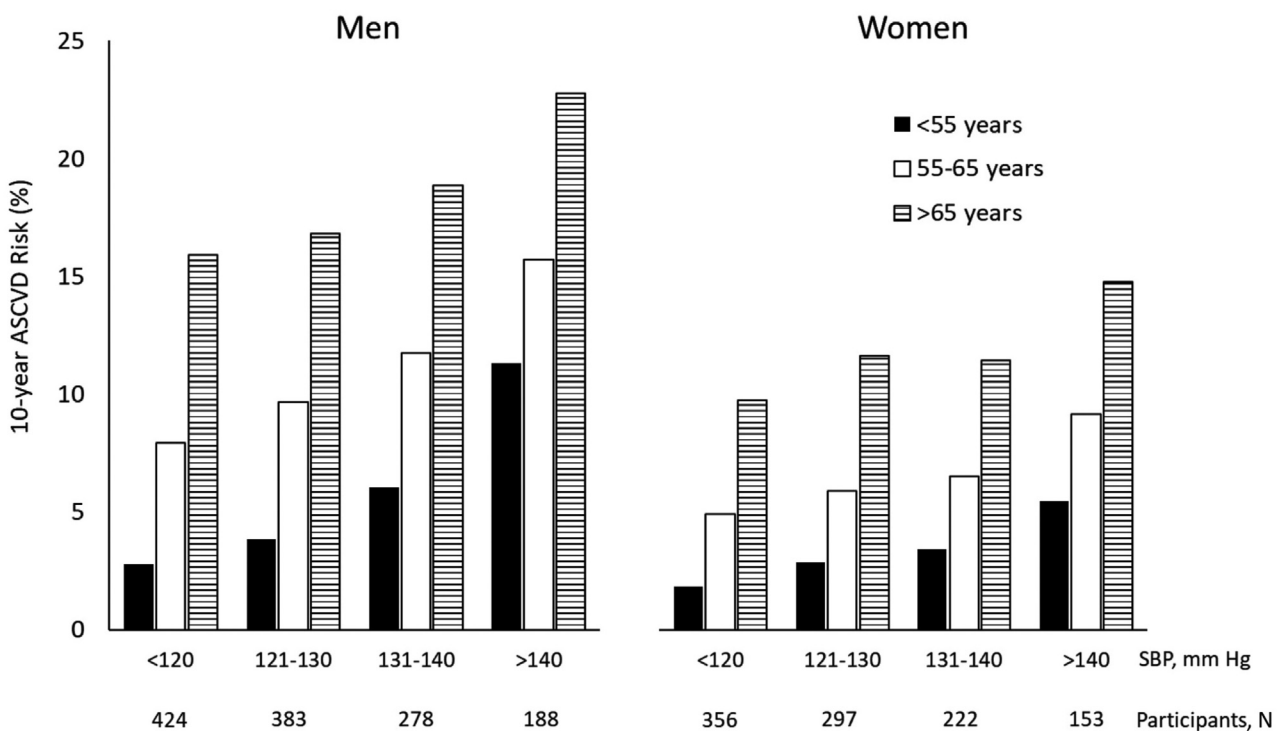


Figure 1: Ten-year ASCVD risk distribution by systolic blood pressure, age, and sex. ASCVD: Atherosclerotic cardiovascular disease; SBP: Systolic blood pressure.

In the NEW2D cohort, the China-PAR model estimated a mean risk of 7.4% of ASCVD events (acute myocardial infarction, stroke, or death from ASCVD) among participants with type 2 diabetes who had not previously received glucose-lowering medication. The risk of ASCVD events among participants in this study was consistent with that in other Chinese cohorts.^[2,5] In the 2016 Chinese guidelines for the management of dyslipidemia in adults, a mean ASCVD risk of 5% to 9% and $\geq 10\%$ was defined as medium and high risk, respectively.^[4] Approximately, half of the participants in this study had an estimated medium or high risk of developing ASCVD within 10 years, supporting the recommendation in the 2016 Chinese guidelines to consider CVD risk lowering medications in newly diagnosed patients with diabetes.^[4] The baseline characteristics that were significantly associated with a risk of developing ASCVD within 10 years included systolic blood pressure, waist circumference, urban living, and age. As systolic blood pressure and waist circumference are modifiable risk factors, they are important targets for prevention and intervention efforts.

The strengths of this study include the relatively large number of participants who were included in the NEW2D cohort and the use of the China-PAR model, which has been validated in a large Chinese cohort and used to predict 10-year risk for ASCVD in four large cohorts in China.^[2] Furthermore, the participants in this study were from 79 hospitals in six major geographic regions in China, representing a diverse cohort with newly diagnosed diabetes. To our knowledge, this is the first population-based study to determine the 10-year ASCVD risk in newly diagnosed patients with type 2 diabetes in China using a validated risk prediction model developed for Chinese populations—the China-PAR model. However, since this study was conducted in the Chinese population, the results may not be generalizable to other ethnic groups, such as Western populations.

In conclusion, approximately half of the participants with type 2 diabetes not receiving glucose-lowering therapy in the nationwide Chinese NEW2D cohort have a medium or high risk of developing ASCVD. Systolic blood pressure and age were found to be the prominent drivers of this elevated risk, which indicated that optimizing blood pressure control might play a key role in reducing ASCVD risk in patients with newly diagnosed type 2 diabetes. The earlier patients adopt appropriate management of ASCVD risk factors, the better prognosis they may have. However, many participants were not treated for ASCVD risk factors. These results underscore the need to intensify lifestyle recommendations and medical treatment of ASCVD risk factors in people with type 2 diabetes in China.

Conflicts of interest

None.

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