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Advances in Cardiovascular Disease Risk Prediction in People with Diabetes

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Abstract

Cardiovascular Disease (CVD) is one of the primary complications in patients with T2DM and a major cause of death among them. However, there are significant differences in CVD risk among patients with T2DM, thus early risk prediction in this population is of critical clinical importance. In this review, CVD is used as an umbrella term; where evidence permits, outcomes are distinguished as atherosclerotic cardiovascular disease (ASCVD; principally coronary heart disease and ischemic stroke), heart failure (HF), or a study-specific composite of major adverse cardiovascular events (MACE). In recent decades, approaches for cardiovascular risk prediction in patients with diabetes have evolved substantially. With advances in medical technology, the ways to predict and assess cardiovascular diseases in this group keep improving. Initially, risk was assessed using just a single risk factor, then multi-indicator joint assessment models appeared, followed by the inclusion of biomarkers and imaging results into the models. In recent years, with the rise of AI algorithms like machine learning (ML) and deep learning (DL), lots of clinical, imaging and omics data have been used for risk prediction. Research has already shown that blood sugar, blood pressure and blood fat levels are linked to cardiovascular events, but the predictive power of a single indicator is limited. The prediction performance of the multi-indicator combined scoring model is better than single-indicator assessment, but when applied to diabetic patients, the model's discrimination and calibration are still not ideal. Biomarkers and imaging may improve risk stratification in selected settings, but evidence that these gains can be generalised across populations or improve clinical outcomes remains limited. ML models can capture nonlinear and longitudinal patterns; however, their incremental value over well-specified statistical models is often modest when the same conventional predictors are used. Reported performance should therefore be compared only when the population, end-

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point definition, prediction horizon, and validation design are sufficiently aligned. This review synthesizes advances in CVD risk prediction for T2DM and examines methodological quality, temporal data leakage, external validation, calibration, fairness, and clinical implementation.

Keywords

T2DM, CVD, Risk Prediction, Machine Learning

1. Introduction

Among patients with type 2 diabetes (T2DM), cardiovascular disease (CVD) is a leading cause of disease burden and premature death. Compared with the general population, patients have approximately a doubled relative risk of coronary heart disease, stroke, and vascular death [1]. In recent years, with developments in medical technology and improvements in diabetes management, the burden of CVD among this population has decreased. However, significant differences in cardiovascular risk persist among patients, and the proportion of patients who achieve the comprehensive risk factor control targets recommended by the guidelines remains low [2]. The clinical characteristics of diabetes-related CVD risk are also changing. In recent years, the incidence of T2DM has been gradually increasing among people under the age of 40. Heart failure has become a major complication for people with T2DM [2]. Studies show that because the risk of CVD varies among different diabetes patients, relying on a single risk assessment method can no longer accurately identify high-risk groups [2] [3]. CVD risk prediction can support risk stratification, risk communication, and shared decision-making. However, treatment selection should follow applicable guidelines and outcome-trial evidence rather than be inferred from prognostic risk estimates alone [2].

With the development of research methods, the CVD risk prediction models for T2DM patients have changed a lot. Early research mainly focused on the relationship between a single risk factor and the risk of CVD. Afterwards, research gradually shifted towards risk prediction models that integrate multiple risk factors, and later included biomarkers and imaging indicators. In recent years, with the development of artificial intelligence technology, machine learning (ML) and deep learning (DL) models have gradually been used for predicting CVD risk, utilising large-scale clinical data, imaging data, and multi-omics data for risk assessment [4]. Compared with the general population, people with T2DM have their risk of CVD influenced more by disease-related factors. Besides the usual risk factors, blood sugar control, the duration of diabetes, and related complications also play a big part in the risk. So, it's still uncertain whether risk prediction models for the general population can accurately assess the CVD risk in T2DM patients, and developing prediction models for this group has become an important direction for future research [5]. This article discusses the development of CVD risk

prediction models for T2DM patients, introduces the features of different types of models and their supporting evidence, and talks about the challenges in future model validation and clinical application.

2. Prediction Based on Single Risk Factors

2.1. Glycaemia and Glucose Variability

Glycemic indicators were among the earliest factors investigated and remain widely used measures for assessing diabetes-related risk. In the UK Prospective Diabetes Study (UKPDS), for every 1% decrease in the mean HbA1c level during the follow-up period, the risk of myocardial infarction decreased by 14%, and the two variables exhibited a continuous linear relationship within the observed range [6]. However, randomised controlled trials show that intensive blood sugar treatment doesn't really improve cardiovascular outcomes. Sulfonylureas or intensified insulin therapy can reduce the risk of microvascular complications, but the risk of heart attack only drops by 16% and isn't statistically significant [7]. In comparison, metformin shows more obvious cardiovascular protective effects in overweight patients, with studies showing it can reduce the risk of heart attack by 39% [8]. The UKPDS 10-Year Follow-up Study further demonstrated that early glycemic control could have persistent effects on later CVD risk, a phenomenon known as the "legacy effect" [9]. In addition, a meta-analysis incorporating more than 100 prospective studies showed that fasting blood glucose levels are associated with a progressively increasing risk of CVD events; patients with T2DM have approximately twice the risk of coronary heart disease, ischemic stroke, and cardiovascular death compared to the general population [1]. In recent years, research has increasingly recognized that relying on a one-time blood glucose level alone to assess CVD risk has certain limitations, and that long-term blood glucose variability can also provide independent prognostic information. A meta-analysis of 12 follow-up studies including 146,653 T2DM patients showed that compared with the group with the lowest HbA1c variability, those in the highest group had a 44% increased risk of CVD events; similar results were also observed for fasting blood glucose variability [10]. Furthermore, in a cohort study involving 8224 adult patients with T2DM, the HbA1c variability score was found to be an independent predictor of new-onset CVD (adjusted risk ratio of 1.70). These studies further show that long-term exposure to risk factors, like variability and cumulative load, might give extra prognostic info beyond single measurements.

2.2. Blood Pressure and Cumulative Exposure

The relationship between blood pressure and the risk of CVD has also been well confirmed. The UKPDS 23 study found that systolic blood pressure is one of five independent risk factors for coronary heart disease in patients with T2DM; other factors include LDL cholesterol, HDL cholesterol, HbA1c, and smoking [11]. The UKPDS 38 study further found that intensive blood pressure control can reduce the risk of stroke by 44% and the risk of microvascular complications by 37% [12].

However, similar to blood glucose levels, a single blood pressure reading does not fully reflect a patient's long-term blood pressure status. In the ACCORD study, cumulative systolic blood pressure (calculated as a weighted average of repeated measurements during the follow-up period) in patients with T2DM independently predicted stroke risk and exhibited a clear dose-response relationship. Compared with baseline systolic blood pressure, cumulative systolic blood pressure has additional predictive value, whereas baseline systolic blood pressure did not independently predict stroke risk after adjusting for other factors [13]. This finding also suggests that, for the assessment of CVD risk, the long-term changes in risk factors may provide more information than a single measurement.

2.3. Lipids and Lipid-Mediated Risk

The UKPDS 23 study found that lipid factors are a key component in research on CVD risk prediction, and that LDL cholesterol is a major modifiable risk factor for coronary heart disease events in patients with T2DM [11]. Then, the Heart Protection Study (HPS) found that, among 5963 patients with diabetes, treatment with simvastatin reduced the risk of major vascular events by 22%, further demonstrating that lipid-related CVD risk in patients with diabetes can be reduced through lipid-lowering therapy [14].

2.4. Limitations of Single-Indicator Risk Assessment

These studies indicate that there is a clear association between individual risk factors and CVD risk, and that these factors have some predictive value. However, depending solely on a single factor for risk assessment has obvious limitations. First, single indicators have limited ability to distinguish between risk levels. Despite certain indicators being closely associated with the onset of CVD, it is difficult to accurately assess risk differences among individuals, with their C-index typically only around 0.60 [15]. This is not simply due to limitations in statistical methods, but rather results from the fact that the onset of CVD is influenced by a combination of factors, and any single factor can only reflect a portion of a patient's overall risk [2]. Second, a single risk factor cannot reflect a patient's overall risk. Even if two patients with T2DM have the same HbA1c level, their future risk of developing CVD may differ significantly if their blood pressure, blood lipid levels, smoking status, and duration of the disease differ [16]. Therefore, while single-marker assessment can identify important risk factors associated with CVD, it cannot accurately assess an individual's overall risk. To more comprehensively integrate information on various risk factors, multifactorial risk prediction models have gradually been developed and are now used to improve the ability to stratify CVD risk.

3. Classical Multi-Factor Risk Scores

3.1. The Framingham Risk Paradigm

The Framingham Risk Score (FRS) was developed in the 1990s. The model takes

into account risk factors such as age, sex, total cholesterol, HDL cholesterol, systolic blood pressure, smoking status and diabetes status. FRS is one of the modern risk scoring models and has influenced the creation of many clinical guidelines over the past 20 years [17]. However, FRS handles diabetes in a fairly simple way, without taking into account the duration of diabetes, blood sugar control levels, or related complications. Research has found that FRS often underestimates the CVD risk in patients with T2DM [18].

3.2. Diabetes-Specific Models: The UKPDS Risk Engine

The UKPDS risk engine is one of the earlier developed and widely used diabetes-specific CVD risk prediction models. The model is based on 4540 UKPDS patients and takes into account factors like age, sex, ethnicity, smoking status, diabetes duration, HbA1c, systolic blood pressure and lipid levels. Unlike previous models that only treated diabetes as a categorical variable, the UKPDS risk engine also takes into account the continuous changes in disease-related indicators, giving a more comprehensive reflection of the risk differences among people with diabetes [19]. The model has advanced the prediction of CVD risk in people with diabetes, making blood sugar control and the duration of diabetes key factors in risk assessment, and it has been used long-term for predicting risk in diabetic populations. However, since this model was developed in the 1990s, its predictive performance might be affected by changes over time. With improvements in diabetes treatment and a decline in CVD incidence, the UKPDS risk engine might overestimate risk in modern populations, a phenomenon known as "risk drift" [5]. Follow-up research found that including diabetes-specific variables can improve the model's predictive ability. However, as clinical treatment patterns and CVD risk levels change, the predictive performance of the UKPDS Risk Engine may be affected, so it needs to be recalibrated regularly [20].

3.3. Contemporary General-Population Risk Scores

In recent years, risk scoring models for the general population have continued to evolve, and the number of predictive variables included has gradually increased. The pooled cohort equations (PCE) of the 2013 ACC/AHA guideline estimated 10-year atherosclerotic CVD (ASCVD) risk in sex- and race-specific models [21], but analyses have documented substantial overprediction in contemporary populations, prompting recalibration efforts [22]. QRISK3 expanded the predictor set to 19 variables—adding ethnicity, chronic kidney disease, systolic blood pressure variability, and other conditions—and was derived and validated in millions of UK primary care records [23]. The SCORE2 algorithms further improved European CVD risk prediction by incorporating competing-risk-adjusted models and regional risk categories [24].

3.4. SCORE2-Diabetes: Development and External Validation

SCORE2 is one of the CVD risk prediction models designed for the general Euro-

pean population; however, its included variables primarily reflect traditional cardiovascular risk factors and do not fully account for disease-specific factors unique to patients with T2DM. Therefore, its application in the T2DM population has certain limitations. To improve risk assessment capabilities for patients with T2DM, researchers developed the SCORE2-Diabetes model based on it. This model was developed using data from 229,460 European patients with T2DM and was externally validated in an independent cohort of 217,036 patients. Based on the traditional risk factors, SCORE2-Diabetes further incorporates three diabetes-related variables—age at diagnosis, HbA1c, and eGFR—enabling the model to better identify differences in risk among patients with T2DM. Compared with SCORE2, SCORE2-Diabetes showed an increase in the C-index of 0.009 to 0.031, suggesting that it has better risk discrimination ability [25]. The 2023 European Society of Cardiology (ESC) guidelines recommend SCORE2-Diabetes for estimating 10-year CVD risk in patients aged ≥ 40 years with T2DM who do not have ASCVD or severe target-organ damage [26]. However, the first independent external validation study in Chinese patients with diabetes found that the original SCORE2-Diabetes model underestimated CVD risk, with risks underestimated by 30% in men and 50% in women. After regional calibration, the model's calibration performance improved significantly while maintaining stable discriminatory power (C-statistic 0.70 - 0.73) [20]. These findings highlight that the applicability of risk prediction models depends not only on model development but also on external validation and appropriate recalibration in target populations.

3.5. Comparison and Limitations of Risk Scoring Models

The development of multifactorial risk scoring models has shown that, compared with a single risk factor, combining multiple variables can improve the ability to assess CVD risk. However, this improvement remains limited, and the ability of these models to calibrate is susceptible to changes in the population. A study of 168,871 patients with T2DM in the United Kingdom compared 22 risk scoring models. The results showed that the AUC values for CVD prediction across all models ranged from 0.62 to 0.67, and more complex models did not significantly improve their ability to distinguish between groups. For example, QRISK3 (19 variables) did not perform better than SCORE (6 variables). In addition, there was no significant difference in discriminatory ability between the T2DM-specific model and the general population model. Although some models performed poorly in terms of calibration across different populations, their predictive results improved significantly after recalibration, suggesting that the models' applicability is influenced by population differences [5]. Although traditional risk-scoring models have certain limitations, diabetes-specific models redeveloped for specific populations still show potential for further optimization. U.S. researchers developed the DMRS model based on 2174 patients with diabetes from four cohorts, incorporating variables such as age, sex, HbA1c, creatinine, systolic blood pressure, use of antidiabetic medications, and smoking status. This model demon-

strated good discriminatory ability in predicting various CVD outcomes (AUC 0.72 - 0.79) and outperformed existing risk scoring models [27]. In addition, risk models tailored to specific clinical outcomes and application scenarios are gradually emerging. For instance, the PRECISE-DM score, which is used to predict coronary artery disease and cardiovascular events in asymptomatic patients with T2DM, has a C-statistic ranging from 0.68 to 0.71, outperforming the UKPDS Risk Engine and the FRS [28]. Meanwhile, the WATCH-DM and TRS-HF (DM) models are used to predict the risk of heart failure in patients with T2DM [29].

Overall, while traditional risk scoring models have improved the ability to assess CVD risk, their performance gains have gradually plateaued. Therefore, researchers have started exploring new risk prediction strategies that integrate biomarkers, imaging, dynamic data, and machine learning methods.

4. The Application of Biomarkers and Imaging in CVD Risk Prediction

4.1. Statistical Metrics for Incremental Predictive Value

Incorporating biomarkers and imaging data into traditional risk models may improve risk stratification in selected settings; however, their incremental value should be assessed in terms of discrimination, calibration, reclassification, and net benefit rather than predictive accuracy alone. In particular, the value of a newly added variable cannot be assessed solely based on changes in the C-statistic, as the C-statistic is not sensitive to minor improvements in the model. Therefore, researchers have proposed methods such as net reclassification improvement (NRI), integrated discrimination improvement (IDI), and decision curve analysis (DCA) to evaluate the impact of newly added variables on risk reclassification and clinical decision-making [30]-[32]. These methods provide an important basis for evaluating the incremental predictive value of biomarkers and imaging information.

4.2. Blood Biomarkers in CVD Risk Prediction

Among blood biomarkers, cardiac-related markers have relatively strong predictive evidence. The BiomarCaRE consortium study included 95,292 participants from European populations, 6090 of whom had diabetes. The study found that, after adjusting for traditional risk factors, hs-cTnI, NT-proBNP, and hs-CRP were all independently associated with CVD events. When these markers were further incorporated into the risk model, the model's C-index increased to 0.81 [33]. The value of biomarkers lies not only in risk prediction but also in their potential to help identify subgroups that respond differently to treatment. A scoring model based on NT-proBNP, history of heart failure, and hs-cTnT can predict the risk of hospitalization for heart failure in patients with T2DM, with C-index values of 0.87 and 0.84 in the development and external validation cohorts, respectively. Further analysis revealed that the absolute benefits of dapagliflozin treatment were more pronounced among the medium- and high-risk patients identified by the model, whereas the benefits for low-risk patients were relatively limited [34].

These findings represent a risk-stratified analysis of treatment-effect heterogeneity and do not establish that the prognostic model can directly select treatment.

4.3. Imaging Markers in CVD Risk Prediction

Among imaging markers, CAC scoring has the most extensive evidence for improving CVD risk stratification in patients with T2DM. Studies have shown that a CAC score of 0 can identify individuals with lower CVD risk despite diabetes. Therefore, CAC scoring may inform risk discussions in selected patients; however, whether its use changes treatment decisions or improves clinical outcomes requires further evaluation [35]. However, the added value of imaging parameters still needs to be evaluated with caution. Although the CAC score can improve risk stratification for some patients, its predictive performance remains influenced by the study population and the evaluation methods used. More importantly, the clinical value of imaging markers depends not only on improvements in the model's statistical performance, but also on whether they can influence clinical decision-making. Therefore, imaging-based risk prediction strategies require further evaluation through external validation and clinical outcome studies [36].

5. Machine Learning and Deep Learning

5.1. Application of Machine Learning Methods in CVD Risk Prediction

In studies predicting CVD risk in patients with T2DM, machine learning (ML) methods are increasingly being used to uncover complex relationships that traditional statistical models struggle to capture. Currently, commonly used methods include regularized regression, random forests, gradient-boosted trees (such as XGBoost and LightGBM), support vector machines, and deep neural networks. Among these, tree-based models have become widely used in clinical data and electronic health records (EHRs) because they can handle different types of variables, missing data, and nonlinear relationships. At the same time, logistic regression remains the benchmark method among traditional statistical models and is used to compare the predictive performance and clinical interpretability of ML models [37]. A systematic review of ML models for predicting cardiovascular complications in T2DM showed that neural network models have high predictive performance, with an AUC as high as 0.91. However, the quality of the research reports remains inadequate, with only 53.75% meeting the TRIPOD criteria, and most studies were found to have a high or unclear risk of bias according to the PROBAST assessment [38]. This implies that, although ML models demonstrate better predictive performance, their reliability is still limited by the quality of the study design and methodology.

5.2. The Application of Machine Learning in Large-Scale Clinical Data

The use of large-scale clinical cohorts and electronic health record (EHR) data has

further advanced the development of ML models for predicting CVD risk in patients with T2DM. In the All of Us Research Program, researchers developed a predictive model based on clinical parameters, electrolyte levels, and biomarker data from 9059 patients with type 2 diabetes mellitus (T2DM) who were treated with SGLT2 inhibitors. Compared with logistic regression, the XGBoost model demonstrated better predictive performance for major adverse cardiovascular events (accuracy: 0.80 vs. 0.65), with the best predictive performance observed for stroke [39]. In a study of more than 300,000 diabetes patients in China, gradient boosting and random forest models were used to predict the risk of coronary heart disease, achieving an AUC of 0.701, indicating that machine learning methods can extract effective predictive information from large-scale clinical data [40]. Similarly, the European Silesia Diabetes-Heart Project study showed that a model built using LightGBM achieved an AUC of 0.740 in predicting CVD events among patients with diabetes and chronic kidney disease, which was higher than that of logistic regression (0.621). Through Shapley additive explanations (SHAP) analysis, the researchers further identified key variables influencing the model prediction, including eGFR, age, and the triglyceride-glucose index [41]. Overall, large-scale cohort studies and EHR research suggest that ML methods can extract potential predictive information from complex clinical data and improve the performance of CVD risk prediction. At the same time, explainable methods like SHAP help identify key predictors in the model, making it easier to apply machine learning models in clinical settings.

5.3. Risk Prediction Based on Longitudinal Data

In recent years, prediction models for CVD risk in T2DM have gradually shifted from relying on single measurements to incorporating long-term dynamic changes. Among 16,378 patients with T2DM in the Kailuan cohort, risk-factor trajectories were derived from repeated measurements collected during a 4-year observation window after cohort enrolment. Participants who experienced a cardiovascular event or were censored during this window were excluded; the end of the observation window therefore served as the prediction index date, after which cardiovascular outcomes were assessed. In the test set, the ML-CVD-C model achieved a C-index of 0.80, outperforming models based only on baseline indicators and traditional risk scores such as China-PAR and PREVENT, which had C-index values of 0.62 - 0.65; the corresponding NRI improvements ranged from 44.1% to 57.7% [42]. This result is consistent with previous findings concerning cumulative blood pressure exposure and blood glucose variability [10] [13]. The above results suggest that longitudinal changes in risk factors can provide additional predictive information beyond baseline measures. When building trajectory models, all repeated-measure data for predictors must be collected prior to the prespecified prediction baseline date; using data collected after the baseline date or during the outcome follow-up period will result in time-related information leakage and overestimate the model's apparent performance.

5.4. Applications of Deep Learning in Multimodal Data

The development of deep learning (DL) has further expanded the data sources for predicting CVD risk, letting models bring together lots of info beyond the usual risk factors. A DL model built from retinal screening images of T2DM patients can predict the risk of major adverse cardiovascular events (MACE) over the next 10 years, and its predictive performance is comparable to the PCE model (both have an AUC of 0.697). After further including PCE scores and coronary heart disease polygenic risk scores, the model's AUC increased to 0.728, suggesting that retinal images might provide vascular risk information independent of genetic factors [43]. DL is also used for automated quantitative image analysis, in addition to retinal imaging. A coronary artery calcification scoring model developed using chest CT images further improved the predictive ability of the Framingham risk score in patients with T2DM, with the C-index in external validation increasing from 0.67 to 0.70 [44]. Furthermore, deep learning models based on the Transformer architecture have begun to be applied to risk prediction in large-scale populations. In a cohort of 156,790 Chinese adults, the China-AIHeart model achieved a C-statistic of 0.767 (for men) and 0.780 (for women), outperforming the Cox model with the same predictor variables, and maintained consistent performance in an independent cohort [45].

5.5. Limitations of Machine Learning Models and Challenges in Clinical Translation

Although ML methods demonstrate strong data processing capabilities, their advantages over traditional risk models still need to be evaluated with caution. Existing research shows that when ML models are compared with traditional models based on the same variables, their discriminatory power typically improves only marginally, and the advantages of some models diminish significantly after external validation and calibration assessments [38]. The 22-score comparison in primary care T2DM found that more complex scores did not outperform simpler ones [5] [38]. The scenarios where ML truly excels primarily include high-dimensional data (such as imageomics and omics data), nonlinear relationships, and long-term dynamic patterns; however, for data containing only a small number of conventional clinical variables, the improvement in predictive performance is often limited. Furthermore, current ML research still faces widespread methodological issues, including a high proportion of internal validation, risks of data leakage, and inadequate reporting standards. A systematic review of ML models for predicting CVD in diabetes showed that, although some neural network models reported high AUC values, most studies still carried a high or unclear risk of bias, and compliance with the TRIPOD reporting criteria was low [38] [42]. Explanatory tools such as SHAP can help identify important predictors in a model, but they cannot replace model validation [41]. Future development of ML models should focus on improving reliability and clinical applicability rather than merely enhancing predictive performance.

6. Model Evaluation and Clinical Translation

6.1. Prediction Model Evaluation and Reporting Standards

Risk prediction models need to be systematically evaluated before they are used in clinical practice. In recent years, the relevant evaluation and reporting standards have been continuously improved. PROBAST can be used to assess the risk of bias and applicability in predictive model studies [46]. The TRIPOD AI statement released in 2024 further improved the reporting guidelines for regression and machine learning models, focusing on model application scenarios, handling of missing data, and external validation. When evaluating a model, you should look at its ability to distinguish as well as how well it's calibrated. Even if a model can tell apart patients with different risk levels, its clinical value is still limited if it can't accurately predict an individual's actual risk [47]. Additionally, DCA can be used to assess the clinical net benefit of the model at different risk thresholds [32].

6.2. Contemporary Evidence: QR4 and PREVENT

In recent years, the latest risk prediction models have been paying more attention to model calibration and how applicable they are across different populations. The development of models like QR4 and PREVENT suggests that expanding the research data, choosing predictive factors wisely, and recalibrating based on the target population can help improve the accuracy of risk predictions [22] [48] [49]. However, the model's performance not only depends on the method itself, but is also influenced by the modelling population, the distribution of risk factors and the application scenario. Carrying out external validation and calibration for different regions and groups is an important step to make sure risk prediction models can be used reliably.

6.3. Clinical Implementation: Risk Communication and Guideline-Concordant Treatment

There are still a few challenges when using risk prediction models in clinical practice. First, the model needs to be integrated with electronic health record systems to enable automated risk assessment; for AI models, issues like data interoperability, regulatory approval and prospective clinical validation also need to be addressed [50]. Furthermore, model fairness is also something we need to keep an eye on for future use. The current risk scores might not fully take socioeconomic factors into account, which can lead to differences in prediction accuracy and healthcare resource allocation among different groups. So, when developing and using models, fairness evaluation should be taken into account [51]. Risk prediction models estimate the probability of future CVD events and may support risk communication and shared decision-making. They should not be interpreted as direct tools for treatment selection; treatment decisions should remain based on applicable guidelines, outcome-trial evidence, contraindications, comorbidities, and patient preferences.

7. Challenges and Future Directions

7.1. Dynamic and Multimodal Risk Prediction

The development of future risk prediction models will gradually shift from static assessments to dynamic, multi-dimensional risk predictions. Traditional models mainly rely on single-time measurements, while longitudinal data can capture how risk factors change over time, providing more information for risk assessment. At the same time, multimodal models that combine clinical indicators, biomarkers, imaging data and other high-dimensional data are likely to achieve more comprehensive and personalised risk assessments. However, these models still need further external validation and clinical utility evaluation before they can be used in clinical practice [42].

7.2. Integration of Omics and Genetic Information

Multi-omics and genetic information offer new approaches to CVD risk prediction. Evidence from T2DM-specific and general-population cohorts suggests that proteomic, metabolomic, and polygenic information may provide incremental predictive information beyond traditional clinical factors; however, the reported improvements are generally modest, and findings from general-population cohorts require independent external validation before being extrapolated to patients with T2DM [52]-[54].

7.3. Validation, Fairness and Clinical Translation

The development of future risk prediction models still needs to tackle some key issues, including data differences between different healthcare systems, insufficient model calibration, inadequate external validation and algorithm fairness. For machine learning models, improving the transparency of research reports, strengthening external validation, and focusing on equity across different populations are key directions for advancing their clinical application [38] [47] [50] [51].

8. Conclusion

Over the past few decades, T2DM patients' CVD risk prediction models have kept evolving, but improvements in the models' ability to distinguish risks are still quite limited. Multifactorial risk scoring models remain the foundation of risk prediction today; their performance is influenced by the study population and the historical context, and therefore their applicability must be improved through external validation and model calibration. Biomarkers and imaging indicators may provide additional information beyond traditional risk factors in selected settings; however, their transportability and ability to improve clinical decision-making or patient outcomes remain uncertain. In recent years, ML and DL technologies have further expanded the sources of data used for risk prediction, and are particularly well-suited for processing high-dimensional data, longitudinal data, and imaging

information. However, the complexity of a model doesn't directly reflect its clinical value; its actual use still depends on thorough external validation, clear research reporting and assessment of clinical benefits. In the future, risk prediction models will continue to evolve toward greater dynamism, multimodality, and intelligence; however, their ultimate value must still be grounded in reliable methodological evaluation, thorough validation, and demonstrated clinical benefits.

Author Contributions

Writing—original draft preparation, Yuhuan Li; writing—review and editing, Junli Xue.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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