Assessment of Atherothrombotic Risk in Patients with Type 2 Diabetes Mellitus

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BACKGROUND

- Risk of atherothrombotic events is not uniform in patients with type 2 diabetes mellitus (T2DM).
- Tailored risk assessment may be useful to guide selection of pharmacotherapies for CV disease prevention in patients with T2DM.
- Most existing CV risk tools have not been designed specifically for patients with T2DM and/or focus on broad composite outcomes.

METHODS

- We developed and validated a clinical risk model for fatal and non-fatal myocardial infarction or ischemic stroke (M/IIS) in a pooled cohort of 42,572 patients with T2DM from 4 TIMI clinical trial cohorts (SAVOR-TIMI 53, DECLARE-TIMI 58, FOURIER (TIMI 59), CAMELLIA-TIMI 61); a total of 2,668 patients experienced MI or IS (Table 1).
- Candidate variables were assessed with multivariable Cox regression, and independent variables were retained in the final clinical risk model based on consistency of forward and backward selection procedures (p<0.05).
- Discrimination assessed using Harrell’s c-index.
- Calibration assessed in the validation cohort both graphically and using the Greenwood–D’Agostino statistic, including in key subgroups of patients with and without established ASCVD.
- Risk categories defined based on predicted 3-year risk of M/IIS (<3%, 3–6%, 6–9%, ≥9%) in patients with T2DM.

RESULTS

- Sixteen clinical variables were independent predictors of M/IIS in our cohort (Table 2).
- The model identified a 10-fold gradient of M/IIS risk between the top vs. bottom risk quintiles in the derivation and validation cohorts (p<0.0001).
- Model discrimination was very good, with c-indices of 0.704 & 0.705 in the derivation and validation cohorts, respectively (Figure 1).
- The model performed well for MI and IS individually (c-indices 0.723 & 0.721, respectively, in validation).
- Cumulative incidence curves within defined 3-year risk categories demonstrated appropriate calibration of the risk model in both the derivation and validation cohorts (Figure 2).
- The model performed well in patients with and without established ASCVD (i.e., secondary and primary prevention cohorts, respectively); importantly, the model was well-calibrated in each of these subgroups (Figure 3).

CONCLUSIONS

- We developed and validated a risk score for atherothrombotic events, leveraging 16 routinely assessed clinical variables, in ~40,000 well-phenotyped patients with T2DM from 4 contemporary TIMI clinical trial cohorts.
- The score has the potential to improve risk assessment and inform clinical decision-making.