Associations of plasma concentrations of MGO-apoB$_{3184-3194}$, a signature peptide of glycated apoB100, with the risk of cardiovascular events in type 2 diabetes

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❶ Introduction

- Lipoprotein metabolism disorders underlying type 2 diabetes (T2D) are important risk factors for atherosclerosis and cardiovascular diseases (CVD).[1]
- Chronic hyperglycemia induces LDL glycation, leading to an increase in their pro-atherogenic properties.[2]
- We have identified a signature peptide of methylglyoxal (MGO)-mediated glycation of the LDL structural protein apoB100: MGO-apoB$_{3184-3194}$.

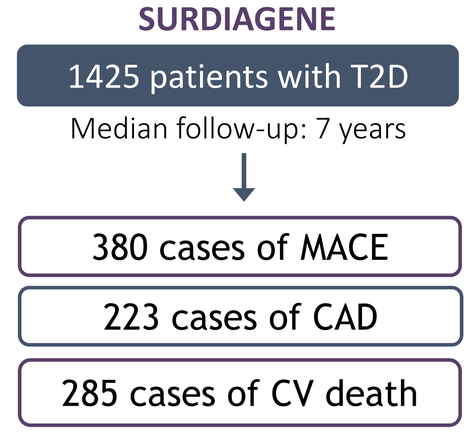
❷ Aim

To evaluate the association of plasma levels of MGO-apoB$_{3184-3194}$ and the risk of CVD in patients with T2D.

❸ Patients & Methods

- The SURDIAGENE study: a single-center cohort of 1425 patients with T2D and without end-stage renal disease.[3]
- Plasma apoB100 and MGO-apoB$_{3184-3194}$ concentrations were simultaneously determined at baseline by mass spectrometry.[4]
- The associations of plasma apolipoprotein concentrations with incident cardiovascular events were evaluated using Cox proportional-hazard models.

Figure 1. Flow chart of study



MACE: Major Adverse CV Events
Stroke ± CV mortality ± myocardial infraction

CAD: Coronary Artery diseases
Myocardial infraction ± coronary artery revascularization

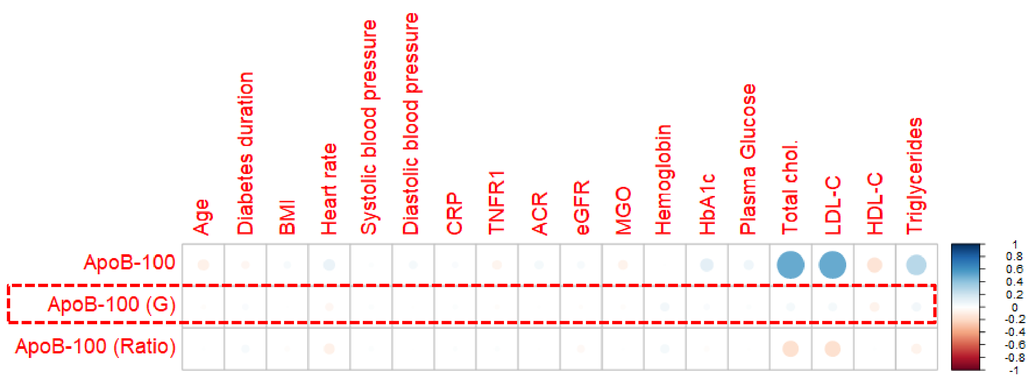
❹ Results

Table 1. Baseline characteristics of participants.

Baseline characteristics	Values
Sex (female)	599/1425 (42%)
Age (y)	65.7 ± 11.7
Diabetes duration (y)	13 [6; 20]
BMI (kg/m²)	31.3 ± 6.3
History of stroke	184/1425 (12.9%)
History of CAD	287/1425 (20.1%)
Active smoker	152/1407 (10.8%)
Heart rate (bpm)	71 ± 14
Systolic BP (mmHg)	132 ± 18
Diastolic BP (mmHg)	72 ± 11
Soluble TNFR1 (ng/mL)	1.84 [1.55; 2.32]
CRP (mg/L)	3.1 [1.4; 7.0]
uACR (mg/mmol)	3 [1; 13]
eGFR (CKD-EPI, mL/min/1.73 m²)	74.4 ± 23.2
HbA_{1c} (%)	7.8 ± 1.5
FPG (g/L)	1.56 ± 0.61
MGO (µmol/L)	0.196 ± 0.087
Total cholesterol (mmol/L)	4.78 ± 1.15
LDL-cholesterol (mmol/L)	2.74 ± 0.96
HDL-cholesterol (mmol/L)	1.21 ± 0.41
Non-HDL cholesterol (mmol/L)	3.57 ± 1.16
Triglycerides (mmol/L)	1.55 [1.11; 2.27]
ApoB100 (µmol/L)	1.59 ± 0.57
MGO-apoB$_{3184-3194}$ (nmol/L)	17.65 [7.22; 32.23]

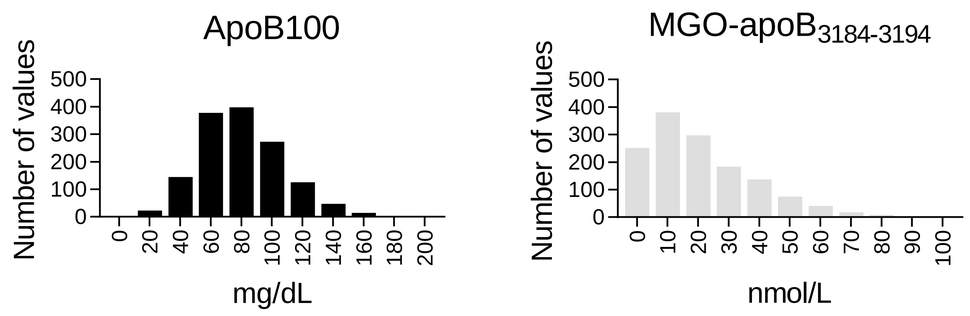
Categorical parameters are expressed as the population size (%). Quantitative parameters are expressed as the mean ± SD (Gaussian distribution), otherwise as the median (IQR).

Figure 2. Spearman correlations of plasma apoB100, MGO-apoB$_{3184-3194}$ and clinical parameters.



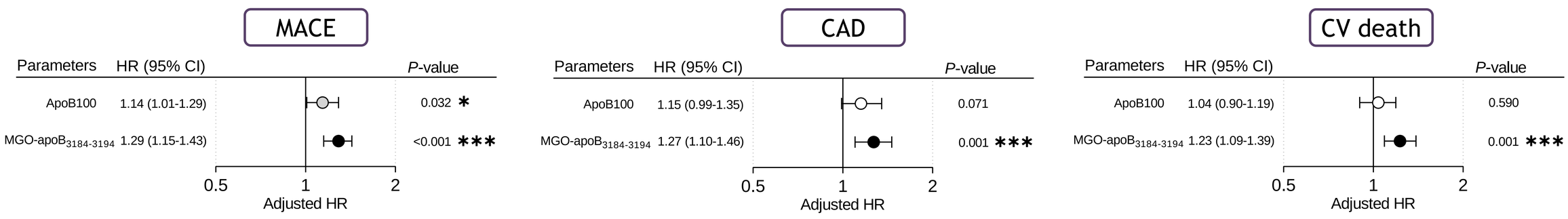
Unlike apoB100, plasma levels of MGO-apoB$_{3184-3194}$ does not correlate with clinical parameters and plasma lipids.

Figure 3. Distribution of plasma concentrations of apoB100 and MGO-apoB$_{3184-3194}$.



Unlike apoB100, plasma levels of MGO-apoB$_{3184-3194}$ does not follow a Gaussian distribution.

Figure 4. Association of plasma apolipoprotein concentrations at baseline with the incidence of CVD in patients with T2D during follow-up.



Hazard ratios (HR) confidence interval (CI) were calculated per 1 SD.

HR were adjusted for predefined risk factors including sex, age, estimated glomerular filtration rate, urine albumin/creatinine ratio, CVD history, HbA_{1c} and non-HDL cholesterol. * $p < 0.05$; *** $p < 0.001$.

- After adjustment, MGO-apoB$_{3184-3194}$ concentrations were significantly associated with the risk of MACE, CAD and CV death.
- These associations remained significant after adjustment for apoB100 concentration.

❺ Conclusion

MGO-apoB$_{3184-3194}$, a signature peptide of MGO-mediated glycation of apoB100, is independently associated with the risk of CV events in patients with T2D, opening new perspectives for its use as a biomarker in clinical practices and epidemiological studies.

References

1. Chen *et al*, *Nat Rev Endocrinol*, 2011
2. Brahimaj *et al*, *Diabetes Care*, 2017
3. Hadjadj *et al*, *Diabetes Care*, 2008
4. Blanchard *et al*, *J Lipid Res*, 2020