VICM, a biomarker of macrophage-driven inflammation, as a risk marker of kidney disease progression in people with type 2 diabetes

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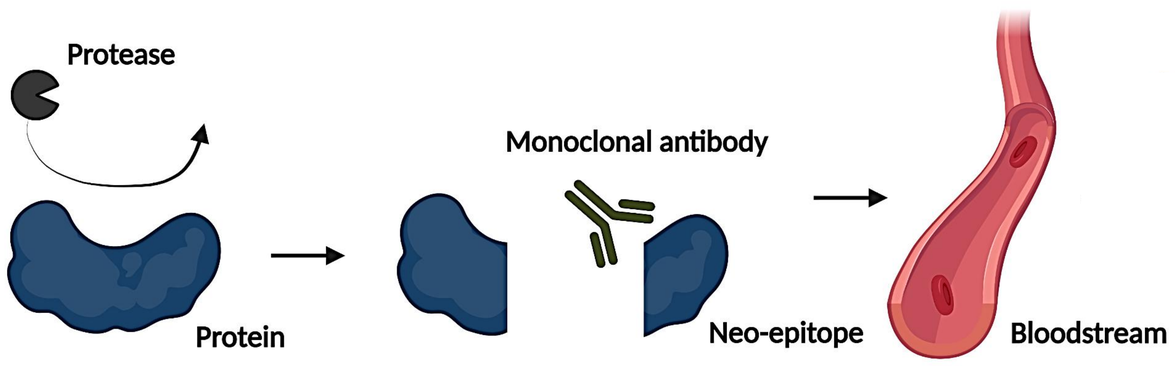
Introduction and Objective

- Hyperglycemia-induced metabolic stress promotes macrophage recruitment, driving inflammation, fibrosis, and kidney damage.
- Early biomarkers that can serve as risk markers for progression of diabetic kidney disease (DKD) are needed.
- We investigated whether circulating VICM—a fragment of citrullinated, MMP-degraded vimentin—is a risk marker for progression of DKD in people with type 2 diabetes (T2D) and moderately increased albuminuria.

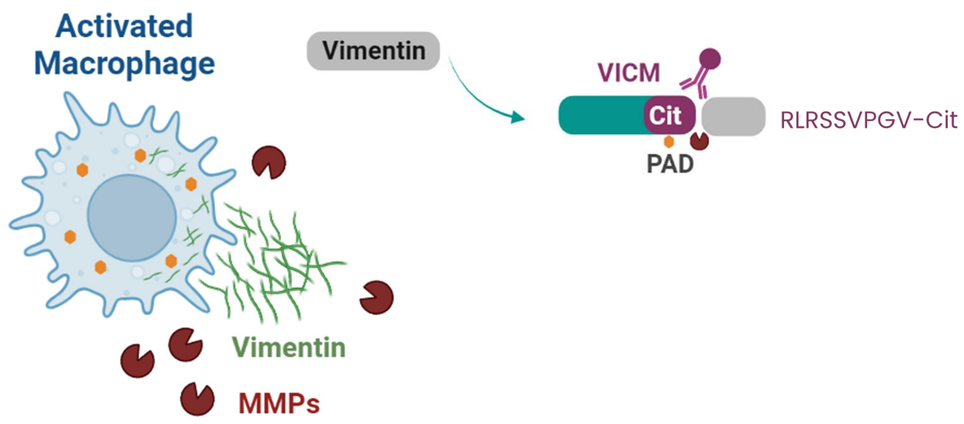
Methods

- VICM was measured at baseline (NordicVICM™ ELISA) in 196 participants with T2D, moderately increased albuminuria, preserved kidney function, moderate inflammatory risk, and no history of cardiac disease enrolled in an observational study conducted at Steno Diabetes Center Copenhagen.
- DKD progression was defined as a ≥30% decline in eGFR. Data on DKD progression were available for 173 (88%) participants.
- Adjusted Cox proportional hazards models were applied.

The Nordic ProteinFingerPrint Technology™



Vimentin is secreted from activated macrophages and citrullinated by PAD, a process that occurs during inflammation



MMP: Matrix metalloproteinase, PAD: peptidylarginine deaminase enzyme.

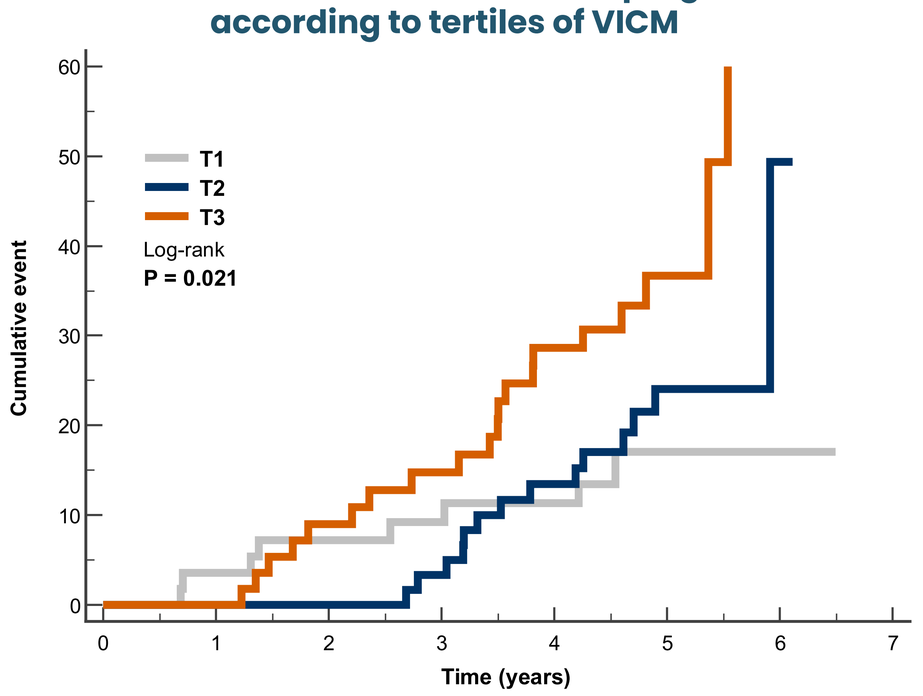
Results

Baseline characteristics

Characteristic	Overall (n = 173)	No DKD progression during follow-up (n = 131)	DKD progression during follow-up (n = 42)	P-value
Age (years)	60 (54-65)	60 (53-65)	60 (56-66)	0.473
Males, n (%)	133 (77%)	101 (77%)	32 (76%)	0.904
Diabetes duration (years)	12 (7-18)	11 (6-18)	13 (8-18)	0.545
BMI (kg/m^2)	32 (29-36)	32 (28-35)	31 (29-36)	0.983
HbA1c (%)	7.5 (6.9-8.8)	7.5 (6.9-8.5)	7.9 (6.6-9.4)	0.689
Systolic BP (mmHg)	129 (119-143)	129 (119-141)	132 (123-144)	0.258
hs-CRP (mg/L)	2.07 (0.87-4.64)	2.01 (0.87-4.02)	2.50 (0.85-8.28)	0.263
TNF-α (pg/mL)	7.9 (6.6-9.6)	7.8 (6.5-9.3)	8.5 (6.9-9.8)	0.262
UAER (mg/24 h)	105 (38-225)	100 (36-192)	143 (53-682)	**0.026**
eGFR (mL/min/1.73 m^2)	90 (77-101)	92 (78-103)	85 (74-93)	**0.016**
VICM (ng/mL)	3.99 (2.98-6.07)	3.78 (2.85-5.74)	4.86 (3.37-8.28)	**0.010**

Data are presented as median (IQR) or number (%). Percentages may sum to more than 100% due to rounding.
P-values are reported for differences between participants with and without DKD progression during follow-up.

Cumulative event curves for DKD progression according to tertiles of VICM



The plot is presented with a truncated y-axis. Median follow was 4.6 years.

Independent association between VICM and DKD progression

	Model 1 HR (95% CI), change in hazard	Model 1 P-value	Model 2 HR (95% CI), change in hazard	Model 2 P-value
VICM	1.56 (1.09-2.25), 56%	**0.016**	1.70 (1.14-2.52), 70%	**0.009**

HRs are reported per doubling.
Model 1: adjusted for age, sex, diabetes duration, BMI, log2-transformed UACR, and eGFR.
Model 2: adjusted for age, sex, diabetes duration, BMI, log2-transformed UACR, eGFR, HbA1c, systolic BP, and log2-transformed hs-CRP.

Conclusion

Higher VICM is an independent risk marker of DKD progression in people with T2D.
Biomarkers reflecting macrophage-driven immune dysregulation, such as VICM, may enable early identification of people at high risk of kidney complications.

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