

Endotrophin as an Early Marker of Kidney Outcomes in Persons with Type 2 Diabetes: Findings from the PROVALID Study

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INTRODUCTION

- Diabetic kidney disease (DKD) is driven by pathophysiological processes, including fibrosis.
- Endotrophin (ETP), a pro-fibrotic fragment generated during collagen type VI formation, has previously been shown to be a biomarker of DKD progression^{1,2,3,4,5}.

AIM

Investigate, for the first time, circulating ETP as a risk marker for kidney outcomes in persons with type 2 diabetes (T2D) being taken care of at the primary level of healthcare.

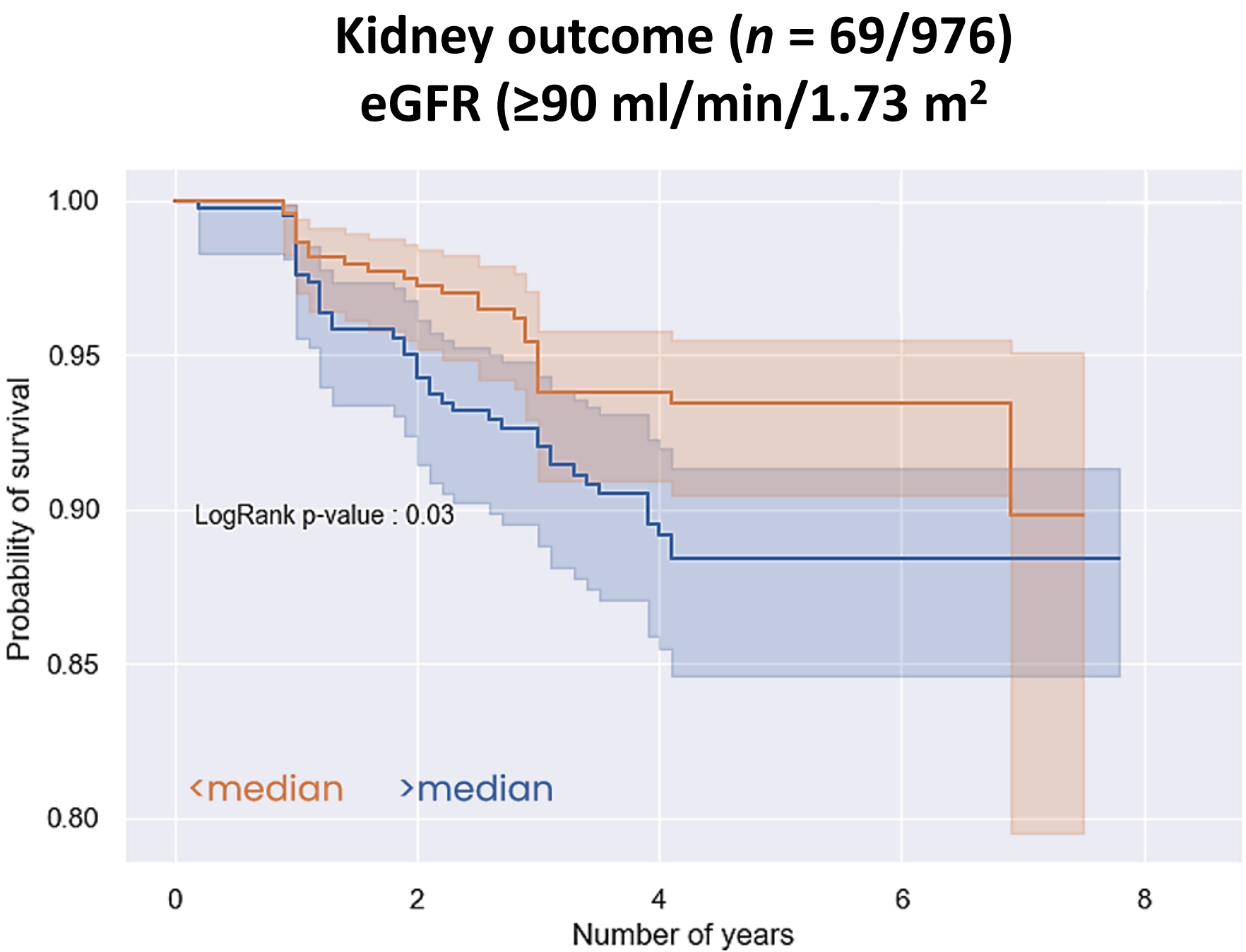
METHOD

- ETP levels were measured using the PRO-C6 ELISA in plasma at baseline from 3226 persons with T2D enrolled in the Prospective Cohort Study in Patients with Type 2 Diabetes Mellitus for Validation of Biomarkers (PROVALID).
- Composite kidney endpoint: Sustained 40% decline in eGFR < eGFR of 60 ml/min/1.73 m², sustained 30% increase in albuminuria, kidney failure, or kidney death.
- Cox proportional hazards regression models: Investigate ETP as a risk marker.
- Kaplan–Meier estimator: Compare the risks according to ETP levels split by median in 976 persons with eGFR ≥90 ml/min/1.73 m².

RESULTS

Baseline characteristics	Overall (n = 3226)
Plasma endotrophin (ng/mL)	9.0 (7.2-11.7)
Age (years)	64 (58-70)
Male sex (%)	1822 (57)
Systolic BP (mmHg)	137 (17)
HbA1c (%)	7.0 (1.2)
Diabetes duration (years)	8 (4-13)
eGFR (ml/min/1.73m ²)	79 (24)
BMI (kg/m ²)	31 (5.4)
Disease history (ASCVD)	1575 (49)

Data are mean (SD), median (IQR), or n (%)

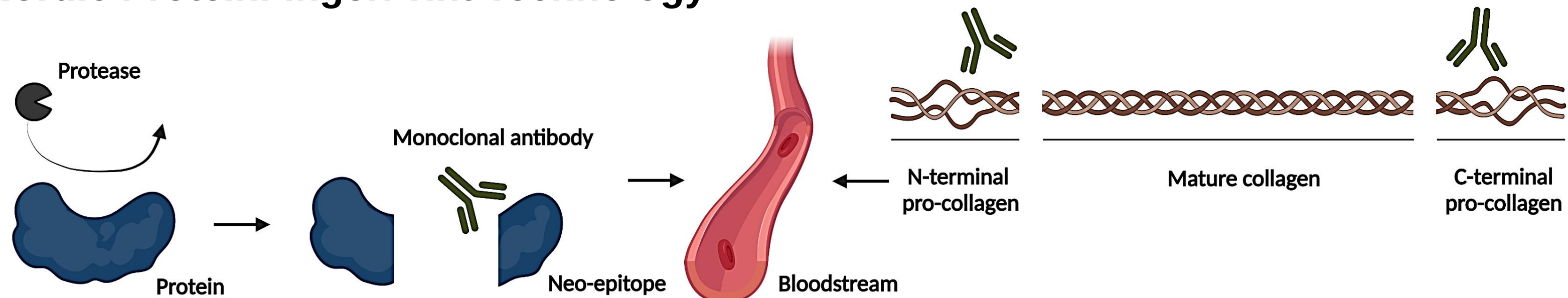


Risks of experiencing the kidney outcome split by baseline median ETP

	Crude		Adjusted*	
	HR (95% CI)	P	HR (95% CI)	P
Kidney outcome (n = 293/3226)	1.63 (1.21-2.19)	0.0012	1.55 (1.13-2.18)	0.012

*Baseline age, systolic BP, HDL, LDL, BMI, eGFR, BMI, HbA1c, diabetes duration, history of ASCVD

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CONCLUSIONS

- Plasma ETP was an independent risk marker for kidney outcomes in persons with T2D with early kidney disease.
- Higher levels of ETP were associated with a significantly increased risk of developing the kidney endpoint in persons with eGFR >90 ml/min/1.73 m².
- These findings demonstrate that markers of fibrosis, such as ETP, may serve as early markers for kidney disease progression or kidney failure in persons with T2D and apparently normal kidney function.

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