Plasmin generation assay in predicting arterial thrombotic outcome in patients with chronic kidney disease

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Northern Health

RESEARCH WEEK 20-24 OCTOBER 2025 INSPIRED RESEARCHERS Northern Health

Background / Aims

Background

- Chronic kidney disease (CKD) is associated with a heightened risk of cardiovascular diseases, in part due to impaired fibrinolysis.
- Plasmin, a protease enzyme, helps dissolve blood clots by degrading fibrin.
- Defect in plasmin generation may lead to excess fibrin formation.

Aims

- To assess the dynamic process of plasmin generation in patients with chronic kidney disease, compared to healthy controls (HC).

Materials & Methods

Demographic

CKD Stage IV & V → 84 recruited
(Defined as eGFR < 30 mL/min/1.73m²)
Healthy Controls (HC) → 143 recruited
(No known cardiovascular risk factors)

Sample Collection

- Sodium citrate specimens were double-spun at 2500g for 10 minutes to obtain platelet-poor plasma.

Laboratory Testing

1. Plasmin generation (PG) was assessed using principles adapted from the calibrated automated thrombogram method for thrombin generation
2. Thrombin Generation (TG)
3. Overall Haemostatic Potential (OHP)

Statistical Analysis

- Differences between groups were assessed using the T-test or Mann–Whitney U test.
- Fine and Gray competing risk model (2 year follow up)

Healthy Controls Vs Chronic Kidney Disease

Table & Figure 1: Comparison of plasmin generation assay parameters between patients with chronic kidney disease (CKD) and healthy controls (HC)

	HC	CKD	P-value CKD vs HC
Lag time (min)	2.33 (2.33-2.67)	2.67 (2.67-2.83)	**<0.001**
Time to peak (min)	4.67 (4.33-5.00)	5.00 (4.67-5.22)	**<0.001**
EPP (nM·min)	263 (203-313)	274 (223-318)	0.24
Peak (nM)	44 (39-52)	44 (40-50)	0.72
Velocity Index (nM/min)	20.30 (17.1-22.7)	20.02 (17.8-22.1)	0.59

Table 1: Results are expressed in median and IQR (Interquartile Range), HC: Healthy Controls, CKD: Chronic Kidney Disease, EPP: Endogenous Plasmin Potential.

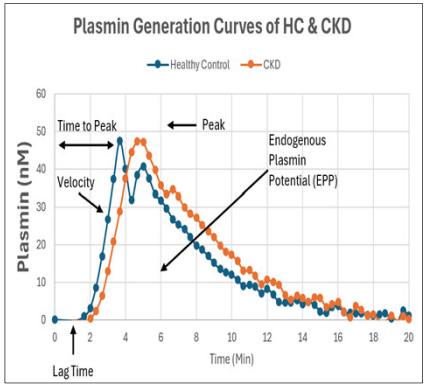


Figure 1: Plasmin generation curves comparing HC against CKD

CKD with more cardiovascular risk factors exhibited delayed plasmin generation

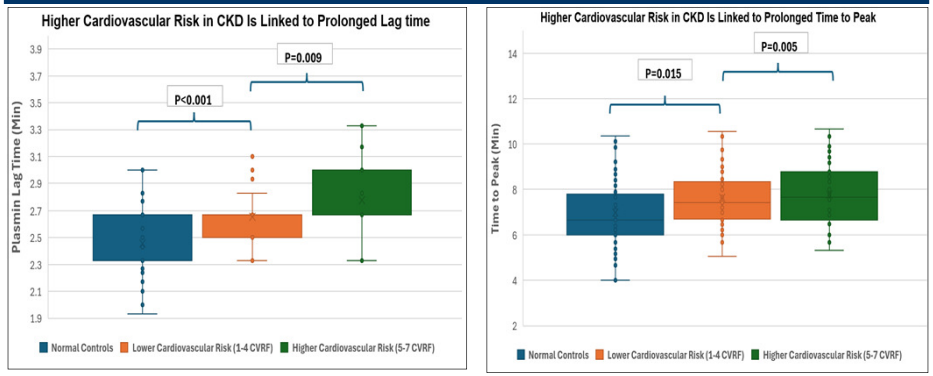


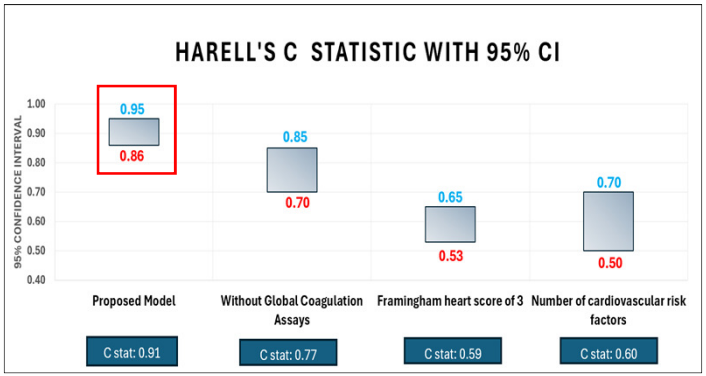
Figure 2A & 2B: Cardiovascular Risk Factors comprise of Hypertension, Obesity, Smoking, Over 65 Years old, Hypercholesteraemia, History of CVD, Family History. P<0.05 is considered as significant.

CKD Demographic	Number
Total Observation	**Total: 84 Patients**
Median Age (IQR)	67 years (58-77)
Male Patients	54 (64%)
Arterial Thrombosis	**Total: 30 patients**
Myocardial Infarction	18
Stroke/Transient Ischaemic Attack	5
Critical Limb Ischaemia	7

Multivariate Competing Risk Regression Model

Variables	Sub hazard Ratio	95% CI	P-Value
OCP:EPP ratio > 0.145	7.43	2.64-20.91	**<0.001**
ttPeak TG:PG > 1.50 min	3.60	1.54-8.42	**0.003**
Plasmin Velocity Index > 20.30 nM·min	5.28	2.25-12.38	**<0.001**
D-Dimer > 820 ng/mL	4.97	1.54-16.02	**0.007**
CRP > 9.95 mg/L	12.50	5.05-30.95	**<0.001**
Framingham heart score of 3	8.02	3.34-19.26	**<0.001**
Competing Risk Regression Model			
Harrell C statistic	**0.91** (0.86 – 0.95)		

Table 2: Risk regression model to predict arterial thrombosis (N=30) in 24 months, competing against mortality (N=7)
Abbreviations: OCP:EPP Fibrin generation/Plasmin Generation Ratio, TG:PG Thrombin generation/Plasmin Generation Ratio, ttpeak: Time to Peak, CRP: C-Reactive Protein. The Youden index was applied to establish the cut-off threshold, P value <0.05 is considered significant.



Summary/Conclusion

- Patients with CKD demonstrated delayed plasmin generation compared to healthy controls.
- CKD patients with delayed plasmin generation exhibited a higher number of concurrent cardiovascular risk factors.
- These findings suggest that altered plasmin generation may contribute to the impaired fibrinolysis in these patients.
- A multimodal risk assessment model incorporating GCAs, including plasmin generation, outperformed traditional models in predicting arterial thrombotic events at 24 months.