Leiden University Medical Center

Chava L. Ramspek[1], Hakan Nacak[1], Merel van Diepen[1], Marjolijn van Buren[2,3], Raymond T. Krediet[4], Joris I. Rotmans[3], Friedo W. Dekker[1]

1 Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands.
2 Department of Internal Medicine, Haga Hospital, The Hague, The Netherlands.
3 Department of Nephrology, Leiden University Medical Center, Leiden, The Netherlands.
4 Department of Nephrology, Academic Medical Center, Amsterdam, the Netherlands.

Pre-dialysis decline of measured GFR but not serum creatinine based estimated GFR is a risk factor for mortality on dialysis.

Background

Monitoring renal function is important in patients with chronic kidney disease (CKD), both for timing the start of renal replacement therapy and determining prognosis. Previous studies in pre-dialysis patients with advanced CKD have shown no or even inverse relations between eGFR decline and mortality.[1] This may be due to the poor validity of serum creatinine-based estimation equations in pre-dialysis patients. Decline in renal function may be better reflected by the mGFR measured as combined creatinine and urea clearance in 24-hour urine samples.[2]

Aim

To explore the effect of fast versus slow mGFR pre-dialysis decline on mortality during dialysis, and to compare the results with the possible effect of fast versus slow eGFR pre-dialysis decline.

Methods

- 197 patients included from NECOSAD
- NECOSAD: prospective multicenter cohort of incident dialysis patients
- Pre-dialysis mGFR and eGFR added from patient records retrospectively

- Inclusion criteria:
  ≥ 2 mGFR values during pre-dialysis
  ≥ 30 days between first and last GFR value

- Individual annual mGFR and eGFR declines were estimated using linear regression. Patients were divided into two categories according to KDOQI:
  fast decline: > 4 mL/min/1.73m² p.a.
  slow decline: ≤ 4 mL/min/1.73m² p.a.

- Survival analyses: Kaplan-Meier curves and Cox proportional hazards regression to adjust for potential confounders

Results

General

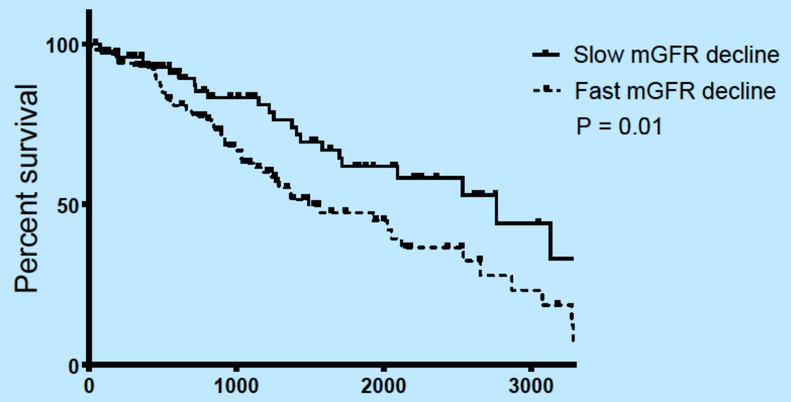
- Fast mGFR decline; N =121
  Slow mGFR decline; N =76
- Characteristics of fast mGFR decliners: more smoking, cardiovascular disease, hypertension, younger, more often male
- Characteristics of slow mGFR decliners: more use of ACE inhibitors, β-blockers, diuretics, more cancer
- Fast eGFR decline; N =111
  Slow eGFR decline; N =86
- 78 (40%) patients died during follow-up (12 years)

Survival and mGFR decline:

In the crude Cox analysis the fast mGFR decline group had a significantly higher risk of death with a hazard ratio (HR) of 1.84 (95%CI: 1.13-2.98) as shown in Figure 1 and Table 1. Model 1 is adjusted for age and gender. When adjusted for the confounders age, gender, primary kidney disease, cardiovascular disease, diabetes, cancer, ethnicity, smoking and, as appropriate, mean mGFR or mean eGFR level in model 2 the HR remained significant at 1.94 (95%CI: 1.11-3.36).

Survival and eGFR decline:

In contrast, no association was found between a fast eGFR decline in the pre-dialysis phase and mortality on dialysis , as shown in Figure 2 and Table 1, the crude HR was 1.20 (0.75-1.89) and the adjusted HR was 1.14 (0.67-1.94).



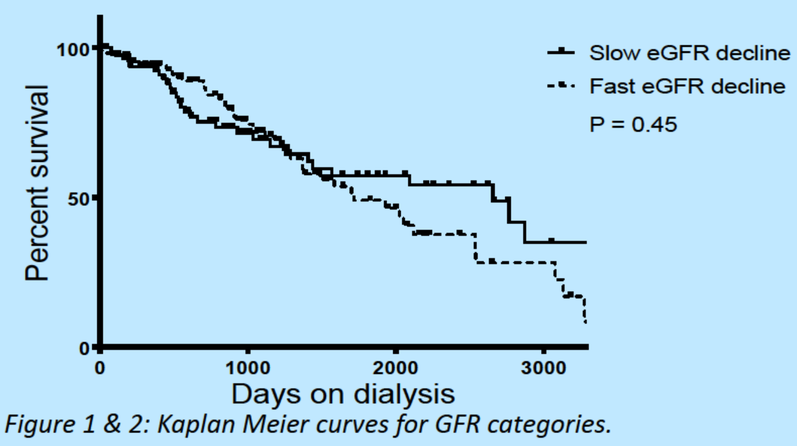


Figure 1 & 2: Kaplan Meier curves for GFR categories.

	mGFR HR (95%CI)	P-value	eGFR HR (95%CI)	P-value
Crude	1.84 (1.13-2.98)	0.01	1.20 (0.75-1.89)	0.45
Model 1	2.14 (1.31-3.48)	0.002	1.06 (0.66-1.70)	0.80
Model 2	1.94 (1.11-3.36)	0.02	1.14 (0.67-1.94)	0.64

Table 1. Results of Cox proportional hazards model for mortality of a fast decline (>4 ml/min/year) compared to a slow decline of mGFR and eGFR (by MDRD).

Discussion

- This is the first study that used mGFR based on 24h urine samples, to study the effect of pre-dialysis decline in renal function on mortality on dialysis.

- Strengths:
  Individual mGFR and eGFR slopes per patient
  Data are representation of everyday clinical practice
- Limitations:
  Retrospective pre-dialysis data
  Possible selection bias

Our results are in line with Haapio et al. who found that fast eGFR decline had no association with a higher mortality after adjusting for confounders.[3]

Conclusions

- A fast mGFR decline during pre-dialysis is an independent risk factor for survival on dialysis, with almost twice as high a mortality rate compared to slow decline.
- This association remains strong when adjusting for multiple confounders.
- In contrast, there was no association found between a fast eGFR decline and mortality on dialysis.

- This study demonstrates the importance of mGFR decline and gives incentive for repeated mGFR measurements in patients on pre-dialysis care as opposed to only assessing eGFR.

References

1)Korevaar JC, Jansen MA, Dekker FW, Jager KJ, Boeschoten EW, Krediet RT, et al. When to initiate dialysis: effect of proposed US guidelines on survival. Lancet. 2001;358(9287):1046-50.
2)Grootendorst DC, Michels WM, Richardson JD, Jager KJ, Boeschoten EW, Dekker FW, et al. The MDRD formula does not reflect GFR in ESRD patients. Nephrology, dialysis, transplantation. 2011;26(6):1932-7.
3)Haapio M, Helve J, Kurimo P, Forslund T, Gronhagen-Riska C, Finne P. Decline in glomerular filtration rate during pre-dialysis phase and survival on chronic renal replacement therapy. Nephrology, dialysis, transplantation. 2012;27(3):1157-63.

Acknowledgments

The nursing staff of the 38 different dialysis units, who collected most of the data, are gratefully acknowledged for their assistance. Moreover, we thank the staff of the NECOSAD trial office for assistance in the logistics of this study.

For any questions please contact Chava L. Ramspek at: c.l.ramspek@lumc.nl

NIERSTICHTING
Leven gaat voor.

53 ERA
302--SP
Chronic Kidney Disease. Clinical Epidemiology.
Chava Ramspek
DOI: 10.3252/pso.eu.53era.2016
ePosters supported by F. Hoffmann- La Roche Ltd.
53rd CONGRESS ERA-EDTA VIENNA AUSTRIA MAY 21st-24th 2016
PosterSessionOnline.com