

Effect of glomerular filtration rate at dialysis initiation on survival in patients with advanced chronic kidney disease: what is the effect of lead-time bias?

Cynthia J Janmaat,¹ Merel van Diepen,¹ Raymond T Krediet,² Marc H Hemmelder,³ Friedo W Dekker¹
On behalf of the NECOSAD study group

¹Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, ²Department of Nephrology, Academic Medical Center, Amsterdam, ³Department of Internal Medicine, Nefrovisie Foundation, Utrecht, Netherlands

Purpose: Current clinical guidelines recommend to initiate dialysis in the presence of symptoms or signs attributable to kidney failure, often with a glomerular filtration rate (GFR) of 5–10 mL/min/1.73 m². Little evidence exists about the optimal kidney function to start dialysis. Thus far, most observational studies have been limited by lead-time bias. The few studies that have accounted for lead-time bias showed contradictory results. We examined the effect of GFR at dialysis initiation on survival in chronic kidney disease patients, and the role of lead-time bias therein. We used both kidney function based on 24-hour urine collection (measured GFR [mGFR]) and estimated GFR (eGFR).

Materials and methods: A total of 1,143 patients with eGFR data at dialysis initiation and 852 patients with mGFR data were included from the NECOSAD cohort. Cox regression was used to adjust for potential confounders. To examine the effect of lead-time bias, survival was analyzed both from the time of dialysis initiation and from a common starting point (GFR 20 mL/min/1.73 m²), using linear interpolation models.

Results: Without lead-time correction, no difference between early and late starters was present based on eGFR (hazard ratio [HR] 1.03, 95% confidence interval [CI] 0.81–1.3). However, after lead-time correction, early initiation showed a survival disadvantage (HR between 1.1 [95% CI 0.82–1.48] and 1.33 [95% CI 1.05–1.68]). Based on mGFR, the potential survival benefit for early starters without lead-time correction (HR 0.8, 95% CI 0.62–1.03) completely disappeared after lead-time correction (HR between 0.94 [95% CI 0.65–1.34] and 1.21 [95% CI 0.95–1.56]). Dialysis start time differed about a year between early and late initiation.

Conclusion: Lead-time bias is not only a methodological problem but also has clinical impact when assessing the optimal kidney function to start dialysis. Therefore, lead-time bias is extremely important to correct for. Taking account of lead-time bias, this controlled study showed that early dialysis initiation (eGFR >7.9, mGFR >6.6 mL/min/1.73 m²) was not associated with an improvement in survival. Based on kidney function, this study suggests that in some patients, dialysis could be started even below an eGFR of 5.7 and mGFR of 4.3 mL/min/1.73 m².