

# 30% GFR decline in 2 years was observed among 62.5% CKD patients initiated hemodialysis: A longitudinal GFR trajectory analysis

Ahmad Baseer Kaihan<sup>1</sup>, Yoshinari Yasuda<sup>1</sup>, Takayuki Katsuno<sup>1</sup>, Sawako Kato<sup>1</sup>, Takahiro Imaizumi<sup>1</sup>, Takaya Ozeki<sup>1</sup>, Koji Inagaki<sup>1</sup>, Manabu Hishida<sup>1</sup>, Naotake Tsuboi<sup>1</sup>, and Shoichi Maruyama<sup>1</sup>

Department of Nephrology, Nagoya University Graduate School of Medicine, Nagoya, Japan

## Introduction and objectives

The established chronic kidney disease (CKD) progression outcome of end-stage renal disease (ESRD) or serum creatinine doubling is a late event requires long observation time and large sample size in clinical research.

GFR decline rate has been highlighted as a new renal outcome for the clinical trial to reduce the sample size and shorten the observation period. We aimed to evaluate the eGFR trajectory among CKD patients initiated hemodialysis (HD).

•Josef Coresh et al; JAMA (2014)

•Matsushita et al; Kidney International (2016)

•Steven J et al; Kidney international (2014)

## Methods

A longitudinal GFR trajectory analysis was conducted among consecutive 112 CKD patients initiated HD between 2014 and 2016 at Nagoya University Hospital. All serum creatinine (SCr) values were collected from the electronic medical record from 2000 to the initiation of HD. Follow-up period was 3 and more SCr measurements in one year. Annual eGFR decline rate (ADR) was calculated by baseline and the last SCr values (Tsai C-W et al; Plos one 12 (4) 2017) and stratified into quartile classification. 30% eGFR decline in 2 year were analyzed in association with eGFR ADR.

Table 1: Baseline clinical characteristics and eGFR annual decline rate (ADR).

| Characteristics   | 1st quartile<br>n=28 | 2nd quartile<br>n=28 | 3rd quartile<br>n=28 | 4th quartile<br>n=28 | P-value       |
|---|----------------------|----------------------|----------------------|----------------------|---------------|
| Annual eGFR decline rate ml/min/1.73 m <sup>2</sup> /yr | 2.9 [1.5-2.4]        | 3.9 [3.5-4.6]        | 6.5 [6.0-8.1]        | 12.0 [10.6-18.2]     | <b>0.0000</b> |
| Men no. (%)   | 23 (79.3)            | 17 (58.6)            | 23 (80.8)            | 23 (79.3)            | 0.19          |
| Age (yr.)   | 65 (57-71)           | 67 (59-73)           | 62.0 (54-71)         | 56 (46-65)           | 0.86          |
| BMI (kg/m <sup>2</sup> )                                | 20.9 (19.3-23.2)     | 21.1 (19.7-23.9)     | 20.6 (19.0-24.9)     | 21.5 (20.0-26.6)     | 0.40          |
| HT no. (%)  | 24 (82.8)            | 26 (89.7)            | 27 (93.1)            | 23 (79.3)            | 0.41          |
| DM no. (%)  | 12 (41.4)            | 14 (48.3)            | 15 (51.7)            | 15 (51.7)            | 0.84          |
| SCr (mg/dL)   | 2.2 (1.5-2.9)        | 1.3 (1.0-2.3)        | 1.04 (0.9-2.2)       | 1.0 (0.7-1.7)        | <b>0.007</b>  |
| eGFR (ml/min/1.73 m <sup>2</sup> )                      | 20.6 (12.8-31.8)     | 40.2 (24.0-54.8)     | 49.3 (24.5-74.7)     | 62.9 (33.3-87.6)     | <b>0.000</b>  |
| UPCR (g/g cr)   | 0.9 (0.5-3.4)        | 2.2 (1.2-3.3)        | 3.3 (1.8-5.8)        | 5.7 (4.3-9.7)        | <b>0.002</b>  |
| Hb (g/dL)   | 11.9 (9.5-12.8)      | 12.7 (11.4-14.1)     | 12.7 (10.3-13.9)     | 12.9 (10.8-14.1)     | <b>0.04</b>   |
| Serum Alb (g/dL)  | 4 (3.7-4.3)          | 4 (3.7-4.3)          | 3.7 (3.4-4.2)        | 3.5 (3.3-3.9)        | 0.25          |
| HbA1C (%)   | 7.3 (6.3-8.1)        | 7.2 (6.3-7.9)        | 7.8 (6.6-9.2)        | 6.8 (6.2-9.8)        | 0.51          |
| SUA (mg/dL)   | 7.7 (7.0-8.7)        | 6.6 (6.0-8.1)        | 6.6 (5.0-7.2)        | 6.4 (5.5-7.3)        | <b>0.03</b>   |
| TCH (mg/dL)   | 174 (149-209)        | 198 (174-227)        | 172 (137-224)        | 203 (171-224)        | 0.56          |
| TG (mg/dL)  | 161 (100-235)        | 143 (123-190)        | 152 (104-241)        | 166 (108-300)        | 0.31          |
| Serum Na (mEq/L)  | 140 (139-141)        | 141 (139-142)        | 140 (139.0-141.5)    | 139.5 (136-142)      | 0.49          |
| Serum K (mEq/L)   | 4.7 (4.5-5.2)        | 4.3 (3.9-4.8)        | 4.5 (4.2-5.1)        | 4.6 (4.2-4.9)        | 0.14          |
| DN (37%)  | 8 (27.6)             | 10 (34.5)            | 11 (37.9)            | 12 (41.4)            | 0.63          |
| NScl (33%)  | 12 (41.4)            | 6 (20.7)             | 9 (31)               | 11 (37.9)            | 0.30          |
| CGN (13%)   | 5 (17.2)             | 4 (13.8)             | 1 (3.4)              | 3 (10.3)             | 0.33          |

Data are expressed no. (%), median (IQR), analyzed by one-way ANOVA, and Kruskal-Wallis H test.

## Results

- The causative kidney diseases were 41 (37%) diabetic nephropathy (DN), 37 (33%) nephrosclerosis (NScl), 14 (13%) chronic glomerulonephritis (CGN), and 20 (18%) others.
- Median follow-up period was 5.6 years. The baseline characteristics of ADR quartiles are shown in Table 1.
- 30% eGFR decline in 2 years were observed in 70 patients (62.5%). Among the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> quartile 13 (46.4%), 16 (57.1%), 18 (64.3%), and 23 (82.1%) patients met 30% eGFR decline in 2 years, respectively. Kaplan-Meier survival curve analysis for 30% eGFR decline revealed significant difference among quartiles [Fig 1].
- The associating factors for eGFR ADR were in SCr, eGFR, protein creatinine ratio (PCR), Hb, and SUA univariate, and eGFR and PCR in multivariate logistic regression analyses [table 2].
- 30% eGFR decline was observed significantly earlier in the greater amount of PCR quartiles [Fig 2]. In GFR categories, G3a has tendency to met 30% eGFR decline later than other GFR categories [Fig3].

Fig 1: Kaplan-Meier survival estimates based on 30% eGFR decline

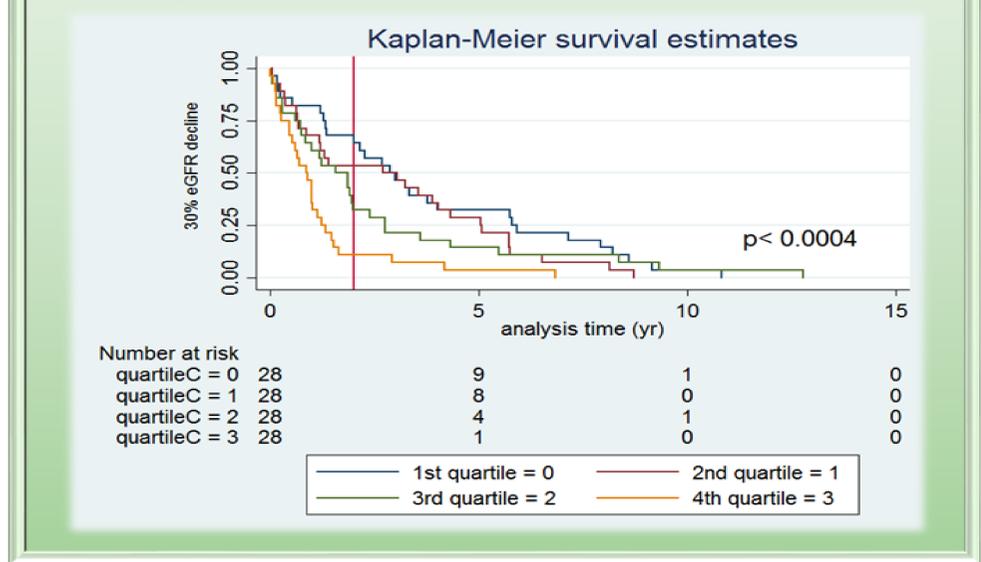


Table 2: Univariate and multivariate logistic regression analysis to annual eGFR decline rate.

| Variables                         | Univariate       |                     | Multivariate      |               |
|-----------------------------------|------------------|---------------------|-------------------|---------------|
|                                   | OR [95% CI]      | P value             | OR [95% CI]       | p value       |
| Age (yr.)                         | 0.98 [0.95-1.02] | 0.34                | 1.02 [0.92-1.12]  | 0.77          |
| Sex (male)                        | 1.22 [0.44-3.42] | 0.70                | 0.75 [0.08-6.72]  | 0.80          |
| BMI (kg/m <sup>2</sup> )          | 1.10 [0.97-1.25] | 0.15                | -                 | -             |
| Hypertension No. (%)              | 2.78 [0.93-8.34] | 0.07                | -                 | -             |
| Serum cholesterol (mg/dL)         | 1.01 [1.00-1.02] | 0.06                | 1.01 [0.99-1.03]  | 0.36          |
| Proteinuria (g/g Cr)              | 2.44 [1.39-4.29] | <b>&lt; 0.002*</b>  | 3.27 [1.20-8.92]  | <b>0.02*</b>  |
| Serum creatinine (mg/dL)          | 0.54 [0.38-0.76] | <b>&lt; 0.0001*</b> | -                 | -             |
| eGFR (ml/min/1.73m <sup>2</sup> ) | 1.08 [1.04-1.12] | <b>&lt; 0.0001*</b> | 1.14 [1.04-1.26]  | <b>0.008*</b> |
| Serum uric acid (mg/dL)           | 0.64 [0.48-0.85] | <b>&lt; 0.002*</b>  | 1.15 [0.65-2.02]  | 0.64          |
| Hemoglobin (g/dL)                 | 1.50 [1.19-1.89] | <b>0.01*</b>        | 0.93 [0.54-1.59]  | 0.78          |
| DM +/-                            | 1.81 [0.73-4.44] | 0.20                | 4.48 [0.62-32.39] | 0.14          |
| DN                                | 1.85 [0.70-4.87] | 0.22                | -                 | -             |
| NScl                              | 0.61 [0.25-1.51] | 0.29                | -                 | -             |
| CGN                               | 0.74 [0.21-2.60] | 0.64                | -                 | -             |

Fig 2: Kaplan-Meier survival estimates of UPCR based on 30% eGFR decline

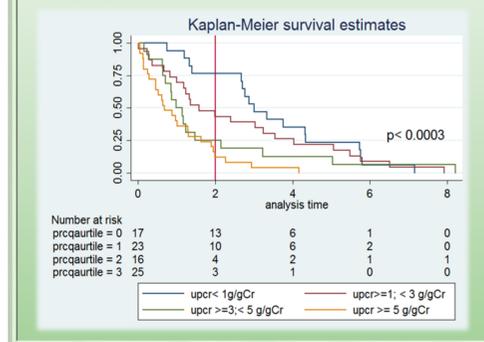
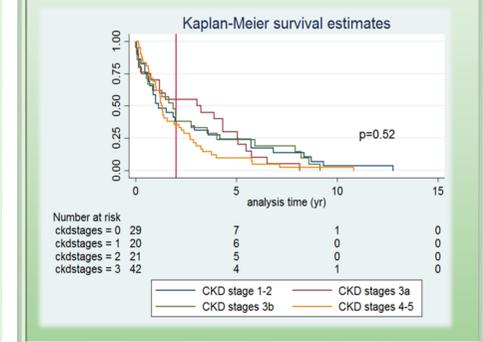


Fig 3: Kaplan-Meier survival estimates based on 30% eGFR in CKD stages



## Discussions

- The eGFR decline rate was significantly faster in the diabetic nephropathy group than that in the nephrosclerosis group (Abe M et al; 5374766, 9 Journal of Diabetes Research 2016).
- Patients with Slow eGFR ADR and individuals with initial CKD stage 3 have longer renal survival for the first 5 years of diagnosis (Tsai C-W et al; Plos one 12 (4) 2017).
- A higher baseline eGFR was related to a faster rate of eGFR decline (Baba M et al; Plos one 10 (6), 2015).

## Conclusion

Although eGFR with 30% decrease in 2 years was earlier renal outcome, approximately 40% of patients initiated HD were negative in this study. The longer observation period should be considered among slowly progressive CKD patients with mild proteinuria and mild-moderately impaired renal function.