**Supplementary Online Content**

Achieved blood pressure and renal outcomes in patients

with advanced stage chronic kidney disease.

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**Statistical analyses – extended**

**General preparations at nephrology clinic for blood pressure measurement and patient’s instruction**

**eTable 1:** (A) Distribution of cohort clinical characteristics over Baseline systolic blood pressure categories. (B) Distribution of cohort clinical characteristics over Baseline diastolic blood pressure categories.

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**Statistical analysis**
Patient characteristics were reported by blood pressure categories at baseline as mean values with standard deviations for normally distributed variables, as medians with interquartile ranges for non-normally distributed variables, and as proportions for categorical variables.Differences between categories were tested using the chi-square test for categorical variables, ANOVA for normally distributed variables, and the Kruskall-Wallis test for non-normally distributed variables.

Linear mixed models were used to model the annual decline in eGFR. A random intercept was included to capture the variation in eGFR baseline value between patients, and a random slope for time to capture variability in the patient eGFR trajectory. Due the non-linear patient trajectories of eGFR, the latter was included as a natural cubic spline. eGFR at baseline was included as a fixed effect. The effect of blood pressure categories at baseline on eGFR decline over time was given by the time – blood pressure interaction parameter. In subsequent models, we investigated this effect adjusted for various groups of *a priori* defined confounders. Analyses were performed on complete cases.

The effect of blood pressure at baseline on time to KRT was modelled using Cox regression, adjusted for various groups of confounders. We also investigated any non-linear effects of blood pressure at baseline on time to KRT using hazard plots in which continuous blood pressure was modelled as a natural cubic spline. The competing risk of death on KRT initiation was described using cumulative incidence functions and dealt with using the cause-specific hazards approach[1].

The effect of blood pressure measured over time on KRT initiation was studied using joint models. The joint model links a linear mixed model, capturing the longitudinal blood pressure measurements, to a separate Cox model, allowing for the estimation of the association between a patient’s blood pressure trajectory and the hazard of starting KRT[2]. A joint model was deemed preferable over a time-dependent Cox model as joint models are capable of dealing with measurement error and non-random drop-out in longitudinal measurements[3]. All analyses were performed in R version 3.4.1.

**General preparations at nephrology clinic for blood pressure measurement and patient’s instruction**

* No talking or use of smartphone during the procedure.
* No exercise, nicotine, or caffeine for at least 15 minutes prior to measurement.
* Remove clothing covering location of cuff.
* Seated comfortably with legs uncrossed and back and arm supported for at least 5 minutes prior to measurement.
* Verify cuff size is correct.

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| **eTable 1 (A)** Distribution of cohort clinical characteristics over Baseline systolic blood pressure categories |
| **Clinical characteristics** |  | overall | Baseline systolic blood pressure |
|  |  |  | <130 | 130–140 | 140–160 | >160 | P-value |
| **Number** |  | 18,071 |  6847 | 3795 | 4888 | 2541 |  |
| **Age(years)(median IQR)** |  |  | 72.8 [63.4, 80.3] | 73.1 [64.2, 80.2] | 73.2 [64.5, 80.3] | 73.5 [65.1, 80.6] | 0.008 |
| **Women** |  |  |  2582 (37.7) |  1390 (36.6) | 1796 (36.7) |  994 (39.1) | 0.148 |
| **Primary renal disease**  | Polycystic kidney disease and other hereditary |  |  317 (4.6) | 191 (5.0) |  221 (4.5) |  81 (3.2) | <0.001 |
| Diabetesnephropathy |  | 1322 (19.3) | 806 (21.2) | 1157 (23.7) | 699 (27.5) |
| Glomerulonephritis |  | 606 (8.9) | 306 (8.1) |  380 (7.8) | 159 (6.3) |
| Hypertensive kidney disease |  | 1771 (25.9) | 1157 (30.5) |  1488 (30.4) | 792 (31.2) |
| Other specified renal diseases |  | 1827 (26.7) | 860 (22.7) | 1082 (22.1) | 521 (20.5) |
| Unknown |  | 1004 (14.7) |  475 (12.5) | 560 (11.5) | 289 (11.4) |
| **Comorbidity**  | Diabetes mellitus |  | 2 085 (30.5) | 1 202 (31.7) | 1 779 (36.4) |  1 009 (39.7) | <0.001 |
| Ischemic heart disease |  | 1 173 (17.1) | 554 (14.6) | 716 (14.6) | 380 (15.0) | <0.001 |
| Chronic heart failure |  | 1 090 (15.6) |  550 (14.5) | 633 (13.0) |  305 (12.0) | <0.001 |
| Cerebrovascular disease |  | 470 (6.9) | 230 (6.1) |  334 (6.8) | 170 (6.7) | 0.409 |
| Peripheral vascular disease |  | 284 (4.1) |  187 (4.9) |  223 (4.6) |  165 (6.5) | <0.001 |
| **Clinical data**  | eGFR (ml/min/1.73m2) (median, IQR) |  | 24.1 [18.4, 29.0] | 23.7 [17.8, 28.7] | 22.7 [16.8, 27.9] | 21.1 [15.4, 27.2] | <0.001 |
| Systolic BP (mmHg) (mean (SD) |  | 120.6 (8.5) | 137.7 (2.8) | 151.6 (5.9) | 177.4 (13.5) | <0.001 |
| Diastolic BP (mmHg) (mean (SD) |  | 71.6 (9.7) | 77.2 (9.88) | 80.1 (11.3) | 86.2 (13.0) | <0.001 |
| BMI (kg/m2) |  | 28.0 (5.8) | 28.4 (5.9) | 28.4 (5.9) | 28.1 (5.7) | <0.001 |
| P-albumin (g/dL) |  | 3.7 (0.5) |  3.7 (0.5) | 3.7 (0.5) |  3.6 (0.5) | <0.001 |
| P-Calcium (mmol/L) |  | 2.3 (0.2) | 2.3 (0.2) | 2.3 (0.2) | 2.3 (0.2) | <0.001 |
| P-CRP (mg/L) (median, IQR) |  | 5.0 [2.2, 10.0] | 5.0 [2.0, 10.0] | 5.0 [2.0, 9.2] | 5.0 [2.00, 9.8] | <0.001 |
| P- Phosphate |  | 1.3 (0.3) | 1.3 (0.3) | 1.3 (0.3) | 1.3 (0.3) | <0.001 |
| B-Hemoglobin (g/dL) |  | 12.1 (1.6) | 12.1 (1.6) | 12.1 (1.6) | 11.9 (1.6) | <0.001 |
| U-albumin/creatinine ratio (mg/mmol) |  | 19.7 [4.1, 93.0] | 30.0 [5.9, 130.6] | 50.0 [9.7, 177.3] | 105.2 [24.5, 260.0] | <0.001 |
| A1(<3mg/mmol) |  | 1370 (20.0) |  593 (15.6) |  586 (12.0) | 164 ( 6.5) | <0.001 |
| A2(3-30mg/mmol) |  | 2549 (37.2) | 1305 (34.4) | 1421 (29.1) |  546 (21.5) |  |
| A3(>30mg/mmol) |  | 2928 (42.8) | 1897 (50.0) | 2881 (58.9) | 1831 (72.1) |  |
| **Medication**  | Erythropoesis stimulating agents |  | 1443 (21.1) |  802 (21.1) | 1084 (22.2) | 596 (23.5) | 0.056 |
| Diuretics |  |  4538 (66.3) | 2429 (64.0) | 3243 (66.3) | 1760 (69.3) | <0.001 |
| Statins |  | 3546 (51.8) | 1978 (52.1) | 2516 (51.5) | 1250 (49.2) | 0.104 |
| ACEi/ARB |  | 3975 (58.1) | 2221 (58.5) | 2942 (60.2) | 1520 (59.8) | 0.092 |

Note: Conversion factors for units: Calcium mmol/L to mg/dL divided by 0.2495; Phosphate mmol/L to mg/dL divided by 0.3229.

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| **eTable 1 (B)** Distribution of cohort clinical characteristics over Baseline diastolic blood pressure categories |
| **Clinical characteristics** |  | overall | Baseline diastolic blood pressure |
|  |  |  | <70 | 70—80  | 80—90  | >90 | P-value |
| **Number** |  | 18,071 | 6140 | 6581 | 3616 |  1734 |  |
| **Age (years) (median IQR)** |  |  | 76.4 [69.3, 82.3] | 73.1 [64.7, 80.0] | 69.4 [58.9, 77.4] | 64.5 [51.0, 73.9] | <0.001 |
| **Women** |  |  | 2509 (40.9) | 2408 (36.6) | 1249 (34.5) | 596 (34.4) | <0.001 |
| **Primary renal disease**  | Polycystic kidney disease and other hereditary |  | 129 (2.1)  | 286 (4.3) |  251 (6.9)  | 144 (8.3) | <0.001 |
| Diabetesnephropathy |  | 1601 (26.1) | 1432 (21.8) |  662 (18.3) |  289 (16.7) |
| Glomerulonephritis |  |  299 ( 4.9) | 553 ( 8.4) | 377 (10.4) | 222 (12.8) |
| Hypertensive kidney disease |  | 1869 (30.4) | 1954 (29.7) | 955 (26.4) | 430 (24.8) |
| Other specified renal diseases |  | 1405 (22.9) | 1491 (22.7) | 939 (26.0) | 455 (26.2) |
| Unknown |  | 837 (13.6) |  865 (13.1) | 432 (11.9) | 194 (11.2) |
| **Comorbidity**  | Diabetes mellitus |  | 2443 (39.8) | 2160 (32.8) | 1032 (28.5) | 440 (25.4) | <0.001 |
| Ischemic heart disease |  | 1259 (20.5) | 966 (14.7) | 420 (11.6) |  178 (10.3) | <0.001 |
| Chronic heart failure |  | 1069 (17.4) |  919 (14.0) | 428 (11.8) | 162 (9.3) | <0.001 |
| Cerebrovascular disease |  | 451 (7.3)  |  433 (6.6) | 218 (6.0) |  102 (5.9) | 0.033 |
| Peripheral vascular disease |  | 360 (5.9) | 303 (4.6) |  130 (3.6) | 66 (3.8) | <0.001 |
| **Clinical data**  | eGFR (ml/min/1.73m2) (median, IQR) |  | 23.3 [17.7, 28.4] | 23.5 [17.7, 28.5] | 23.0 [17.2, 28.3] | 22.7 [16.4, 28.2] | <0.001 |
| Systolic BP (mmHg) (mean (SD) |  | 131.1 (18.5) | 139.3 (18.2) | 148.5 (18.5) | 162.7 (21.9) | <0.001 |
| Diastolic BP (mmHg) (mean (SD) |  | 64.6 (5.9) | 77.8 (2.8) | 86.6 (2.9) | 99.2 (6.8) | <0.001 |
| BMI (kg/m2) |  | 28.1 (5.7) | 28.3 (5.8) | 28.3 (5.9) | 28.1 (5.9) | 0.222 |
| P-albumin (g/dL) |  | 3.6 (0.5) | 3.7 (0.5) | 3.7 (0.5) | 3.6 (0.5) | <0.001 |
| P-Calcium (mmol/L) |  | 2.3 (0.2) | 2.3 (0.2) | 2.3 (0.2) | 2.3 (0.2) | <0.001 |
| P-CRP (mg/L) (median, IQR) |  | 5.0 [2.5, 10.1] | 5.0 [2.0, 10.0] | 5.0 [2.0, 9.1] | 5.0 [2.00, 9.6] | <0.001 |
| P- Phosphate |  | 1.3 (0.3) | 1.3 (0.3) | 1.3 (0.3) | 1.3 (0.3) | <0.001 |
| B-Hemoglobin (g/dL) |  | 11.8 (1.5) | 12.2 (1.6) | 12.3 (1.6) | 12.4 (1.7) | <0.001 |
| U-albumin/creatinine ratio (mg/mmol) |  | 23.0 [4.8, 112.0] | 34.3 [6.2, 136.3] | 49.0 [9.8, 175.3] | 82.3 [17.7, 244.1] | <0.001 |
|  | A1(<3mg/mmol) |  | 1107 (18.0) | 1048 (15.9) | 429 (11.9) |  129 (7.4) | <0.001 |
|  | A2(3-30mg/mmol) |  | 2230 (36.3) | 2100 (31.9) | 1062 (29.4) | 429 (24.7) |  |
|  | A3(>30mg/mmol) |  | 2803 (45.7) | 3433 (52.2) | 2125 (58.8) | 1176 (67.8) |  |
| **Medication**  | Erythropoesis stimulating agents |  | 1476 (24.0) | 1374 (20.9) | 734 (20.3) |  341 (19.7) | <0.001 |
| Diuretics |  | 4513 (73.5) | 4335 (65.9) | 2147 (59.4) |  975 (56.2) | <0.001 |
| Statins |  | 3442 (56.1) | 3418 (51.9) | 1689 (46.7) | 741 (42.7) | <0.001 |
| ACEi/ARB |  | 3595 (58.6) | 3820 (58.0) | 2194 (60.7) | 1049 (60.5) | 0.032 |

Note: Conversion factors for units: Calcium mmol/L to mg/dL divided by 0.2495; Phosphate mmol/L to mg/dL divided by 0.3229.

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| **eTable2.** Annual decline in eGFR by blood pressure category at baseline, and by albuminuria categories, merging A1 and A2 categories. |
| **BP mmHg** | **A1 and A2\*** | **A3\*** |
| **Systolic** | eGFR(ml/min/1.73m2/year) [95% CI] | P-value | eGFR(ml/min/1.73m2/year) [95% CI] | P-value |
| **<130** | -0.65 (-0.76 - -0.54 ) | Ref | -1.54(-1.64- -1.41) | Ref |
| **130-140** | -0.93 (-1.08 - -0.78 ) | 0.003 | -2.01(-2.18- -1.84) | <0.0001 |
| **140-160** | -1.01(-1.16- -0.87) | 0.0001 | -2.22(-2.36- -2.07) | <0.0001 |
| **>160** | -1.05(-1.31- -0.80) | 0.004 | -2.23(-2.41- -2.04) | <0.0001 |
|  |
| **Diastolic** |  |
| **<70** | -0.58(-0.69- -0.46) | Ref | -1.60(-1.75- -1.45) | Ref |
| **70-80** | -0.89(-1- -0.77) | 0.0002 | -1.89(-2.01- -1.76) | 0.003 |
| **80-90** | -1.08(-1.25- -0.91) | <0.0001 | -2.11(-2.27- -1.95) | <0.0001 |
| **>90** | -1.15(-1.4- -0.89) | 0.0001 | -2.64(-2.87- -2.42) | <0.0001 |
| \*Adjusted for baseline eGFR, sex, age group, primary renal disease, diabetes, ischemic heart disease, heart failure, cerebrovascular disease, peripheral vascular disease, diuretics, Angiotensin converting enzyme inhibitor, albumin, calcium, phosphate, hemoglobin. |

**eTable 3:** Annual decline in eGFR by blood pressure category at baseline, and by presence/absence of diabetes.

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| --- | --- | --- |
| **Blood pressure (mmHg)** | **Diabetes (HR; 95% Confidence interval)**  | **No diabetes (HR; 95% Confidence interval)**  |
| **Systolic BP** |  | **P-value** |  | **P-value** |
| **<130** | -1.07 (-1.24 - -0.9 ) | Ref | -0.97 (-1.07 - -0.88) | Ref |
| **130<140** | -1.74 (-1.96 - -1.51 ) | 0.0002 | -1.29 (-1.42 - -1.15)  | 0.0003 |
| **140<160** | -2.05 (-2.24 - -1.86)  | <.0001 | -1.46 (-1.58 - -1.34)  | <0.0001 |
| **≥160** | -2.70 (-2.97 - -2.43)  | <.0001 | -1.41 (-1.60 - -1.23) | 0.0001 |
| **Diastolic BP** |  |  |  |  |
| **<70** | -1.34 (-1.50 - -1.19)  | Ref | -0.80 (-0.92 - -0.69) | Ref |
| **70<80** | -1.81 (-1.98 - -1.64)  | <0.001 | -1.19 (-1.29 - -1.09)  | <0.0001 |
| **80<90** | -2.01 (-2.27 - -1.76)  | <0.001 | -1.51 (-1.64 - -1.38)  | <0.0001 |
| **≥90** | -2.84 (-3.24 - -2.45)  | <0.001 | -1.78 (-1.97 - -1.59)  | <0.0001 |

**eTable 4:** Hazard ratios for time to KRT initiation by baseline blood pressure. adjusted for various groups of confounders.

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| --- | --- | --- |
| **Blood pressure (mmHg)** | **Unadjusted Model** | **Full model\*** |
| **Systolic BP** |  |  |
| **<130** | Ref | Ref |
| **130<140** | 1.27 (1.16-1.38)  | 1.31 (1.20-1.42)  |
| **140<160** | 1.60 (1.49-1.73)  | 1.62 (1.54-1.84)  |
| **≥160** | 1.84 (1.69-2.01)  | 1.82 (1.67-1.99)  |
| **Diastolic BP** |  |  |
| **<70** | Ref | Ref |
| **70<80** | 1.32 (1.23-1.43)  | 1.20 (1.11-1.30)  |
| **80<90** | 1.74 (1.60-1.89)  | 1.34 (1.23-1.46)  |
| **≥90** | 2.19 (1.99-2.41)  | 1.52 (1.37-1.78)  |

\* Adjusted for baseline eGFR, sex, age group, primary renal disease, diabetes, ischemic heart disease, heart failure, cerebrovascular disease, peripheral vascular disease, diuretics, Angiotensin converting enzyme inhibitor, albumin, calcium, phosphate, hemoglobin.

**eTable 5:** Missing data at baseline

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| Clinical characteristics |  | Missing (%) |
| **Overall** | 18 071 | 0.0 |
| **Age**  |  | 0.0 |
| **Women** |  | 0.0 |
| **Primary renal disease**  |  | 0.0 |
| **Comorbidity**  | Diabetes mellitus | 11.3 |
| Ischemic heart disease | 14.4 |
| Chronic heart failure | 14.4 |
| Cerebrovascular disease | 14.4 |
| Peripheral vascular disease | 14.4 |
| **Clinical data**  | eGFR (ml/min/1.73m2) (median, IQR) | 0.0 |
| Systolic BP (mmHg) | 0.0 |
| Diastolic BP (mmHg) | 0.0 |
| BMI (kg/m2) | 39.9 |
| P-albumin (g/dL) | 6.1 |
| P-Calcium (mmol/L) | 11.6 |
| P-CRP (mg/L) (median, IQR) | 26.1 |
| P- Phosphate | 8.3 |
| B-Hemoglobin (g/dL) | 3.3 |
| U-albumin/creatinine ratio (mg/mmol) | 52.2 |
| **Medication**  | Erythropoesis stimulating agents | 7.1 |
| Diuretics | 7.1 |
| Statins | 7.1 |
| ACEi/ARB | 7.1 |

Note: Conversion factors for units: Calcium mmol/L to mg/dL divide by 0.2495; Phosphate mmol/L to mg/dL divide by 0.3229.

**eFigure 1: Flow chart**



BP blood pressure. eGFR estimated glomerular filtration rate. SBP systolic blood pressure. KRT kidney replacement therapy.

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