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## Appendix-Text, Table and Figures

## Appendix-Text S1. Calculation of CLurea, Total body water and nPCR dial + renal

1. CLurea

$$
\text { CLurea }(\mathrm{mL} / \mathrm{min})=\frac{\text { urinary urea }(\mathrm{mg} / \mathrm{dL}) \times \text { urinary volume }(\mathrm{mL})}{\text { collected time }(\mathrm{min}) \times[0.9 \times \text { serum urea }(\mathrm{mg} / \mathrm{dL})]}
$$

2. Correction equation for $\operatorname{BUN}(\mathbf{C o})$ in $\mathbf{n P C R}_{\text {dial+renal }}$
A. For patients who received hemodialysis three times in the preceding week of the $\mathrm{spKt} / \mathrm{V}$ measurement:

$$
C_{0}=B U N \times\{1+(0.70+3.08 /(s p K t / V)) \times \text { CLurea } / T B W\}
$$

B. For patients who received hemodialysis two times in the preceding week of the spKtV measurement:

$$
C_{0}=B U N \times\{1+(1.15+4.56 /(s p K t / V)) \times C L u r e a / T B W\}
$$

3. Total body water (TBW)

For male;

$$
\text { TBW }=2.447-(0.09156 \times \text { Age })+(10.74 \times \text { Height in meters })+(0.3362 \times \text { Postdialysis Weight })
$$

For female;

$$
\text { TBW }=-2.097+(10.69 \times \text { Height in meters })+(0.2466 \times \text { Postdialysis Weight })
$$

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4. $\mathrm{nPCR}_{\text {dial }+ \text { renal }}$
A. For patients who received hemodialysis three times in the preceding week of the $\mathrm{spKt} / \mathrm{V}$ measurement:

For those measurements at beginning of week (M or T);

$$
\text { Calculated } \mathrm{nPCR}=\frac{C_{0}}{\{36.3+5.48 \times(s p K t / V)+53.5 /(s p K t / V)\}}+0.168
$$

For those measurements at midweek (W or Th);

$$
\text { Calculated nPCR }=\frac{C_{0}}{\{25.8+1.15 \times(s p K t / V)+56.4 /(s p K t / V)\}}+0.168
$$

For those measurements at end-of-week (F or Sa);

$$
\text { Calculated } \mathrm{nPCR}=\frac{C_{0}}{\{16.3+4.30 \times(s p K t / V)+56.6 /(s p K t / V)\}}+0.168
$$

B. For patients who received hemodialysis two times in the preceding week of the spKtV measurement:

For those measurements at beginning of week (M or T or W);

$$
\text { Calculated } \mathrm{nPCR}=\frac{C_{0}}{\{48.0+5.14 \times(s p K t / V)+79.0 /(s p K t / V)\}}+0.168
$$

For those measurements at end-of-week (Th or F or Sa);

$$
\text { Calculated } \mathrm{nPCR}=\frac{C_{0}}{\{33.0+3.60 \times(s p K t / V)+83.2 /(s p K t / V)\}}+0.168
$$

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Appendix-Table S1. The baseline characteristics between included (with nPCR dialtrenal $^{\text {data) and excluded (without }}$ $\mathbf{n P C R}_{\text {dial+renal }}$ data) patients of this study in 105,362 incident patients

| Variable | Included patients <br> $(\mathbf{n}=\mathbf{3 6 , 7 5 7 )}$ | Excluded patients <br> $(\mathbf{n}=\mathbf{6 8 , 6 0 5})$ | StdDiff. |
| :--- | :---: | :---: | :---: |
| Age (years) | $62 \pm 15$ | $63 \pm 15$ | 0.08 |
| Women (\%) | 37 | 47 | 0.21 |
| Race / ethnicity (\%) | 54 |  |  |
| Non-Hispanic white | 28 | 43 | 0.22 |
| African-American | 11 | 33 | 0.12 |
| Hispanic | 3 | 37 | 0.17 |
| Asian | 47 | 46 | 0.02 |
| ESRD Reason (\%) | 28 | 30 | 0.02 |
| Diabetes | 10 | 9 | 0.04 |
| Hypertension | 2 | 14 | 0.03 |
| Glomerulonephritis | 13 | 14 | 0.04 |
| Cystic Kidney Disease | 74 | 76 | 0.02 |
| Others | 18 | 14 | 0.05 |
| Access type (\%) | 4 | 4 | 0.12 |
| Central Venous Catheter |  |  | 0.03 |
| AV Fistula | 50 | 52 | 0.03 |
| AV Graft | 38 | 36 | 0.04 |
| Comorbidity (\%) | 2 | 2 | 0.02 |
| Hypertension | 2 | 2 | 0.01 |
| Congestive Heart Failure | $1.55 \pm 0.36$ | $1.42 \pm 0.29$ | 0.39 |
| Cerebrovascular disease |  |  |  |
| History of Cancer |  |  |  |
| spKt/V |  |  |  |
|  |  |  |  |
|  |  |  |  |

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| Body Mass Index $\left(\mathrm{kg} / \mathrm{m}^{2}\right)$ | $27.4(23.6,32.7)$ | $26.3(22.7,31.2)$ | 0.18 |
| :--- | :---: | :---: | :---: |
| Laboratories |  |  |  |
| Hemoglobin (g/dL) | $11.2 \pm 1.1$ | $11.1 \pm 1.2$ | 0.18 |
| Albumin (g/dL) | $3.57 \pm 0.46$ | $3.48 \pm 0.48$ | 0.19 |
| Corrected Calcium (mg/dL) | $9.1 \pm 0.5$ | $9.1 \pm 0.6$ | 0.07 |
| Phosphorus (mg/dL) | $5.0 \pm 1.1$ | $4.9 \pm 1.1$ | 0.09 |
| Creatinine $(\mathrm{mg} / \mathrm{dL})$ | $5.9 \pm 2.4$ | $5.9 \pm 2.4$ | 0.00 |
| Ferritin $(\mathrm{ng} / \mathrm{mL})$ | $268(157,451)$ | $289(168,496)$ | 0.09 |
| Bicarbonate $(\mathrm{mEq} / \mathrm{L})$ | $23.5 \pm 2.6$ | $23.7 \pm 2.7$ | 0.07 |

Note: continuous values are expressed as mean $\pm$ SD if normally distributed or median (interquartile range) if skewed. Differences in patient characteristics between two groups were compared by Std Diff, of which $0.8,0.5$, and 0.2 were considered large, medium, and small differences, respectively, and $\geq 0.1$ was defined as meaningful imbalance.
Abbreviations: AV Fistula, arteriovenous fistula; AV Graft, arteriovenous graft; spKt/V, single pool Kt/V; Std Diff, standardized difference.

Appendix-Table S2. Association between baseline nPCR dial+renal and five-year mortality in 36,757 incident patients

| All-cause mortality | Unadjusted |  | Case-mix adjusted |  | Case-mix and MICS adjusted |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Baseline $n P C R_{\text {dial }+ \text { renal }}$ (g/kg/day) | $\begin{aligned} & \text { Hazard Ratio } \\ & \text { (95\% confidence } \\ & \text { interval) } \\ & \hline \end{aligned}$ | $P$ value | $\begin{aligned} & \text { Hazard Ratio } \\ & \text { (95\% confidence } \\ & \text { interval) } \\ & \hline \end{aligned}$ | $P$ value | $\begin{aligned} & \text { Hazard Ratio } \\ & \text { (95\% confidence } \\ & \text { interval) } \\ & \hline \end{aligned}$ | $P$ value |
| < 0.6 | 1.54 (1.41-1.68) | <0.001 | 1.57 (1.43-1.71) | <0.001 | 1.25 (1.14-1.37) | <0.001 |
| $0.6 \leq$ and $<0.7$ | 1.30 (1.20-1.42) | <0.001 | 1.27 (1.16-1.38) | <0.001 | 1.14 (1.05-1.24) | 0.002 |
| $0.7 \leq$ and $<0.8$ | 1.12 (1.03-1.21) | 0.005 | 1.11 (1.03-1.21) | 0.006 | 1.03 (0.95-1.11) | 0.48 |
| $0.8 \leq$ and $<0.9$ | 1.00 | NA | 1.00 | NA | 1.00 | NA |
| $0.9 \leq$ and $<1.0$ | 0.92 (0.85-0.99) | 0.03 | 0.92 (0.85-1.00) | 0.047 | 0.94 (0.87-1.02) | 0.13 |
| $1.0 \leq$ and $<1.1$ | 0.91 (0.83-0.98) | 0.02 | 0.90 (0.83-0.98) | 0.01 | 0.94 (0.86-1.02) | 0.13 |
| $1.1 \leq$ and $<1.2$ | 0.82 (0.75-0.90) | <0.001 | 0.85 (0.78-0.93) | <0.001 | 0.89 (0.81-0.98) | 0.02 |
| $1.2 \leq$ and $<1.3$ | 0.75 (0.67-0.83) | <0.001 | 0.78 (0.70-0.86) | <0.001 | 0.81 (0.73-0.90) | <0.001 |
| $1.3 \leq$ and $<1.4$ | 0.73 (0.65-0.83) | <0.001 | 0.75 (0.66-0.85) | <0.001 | 0.79 (0.69-0.89) | <0.001 |
| $\geq 1.4$ | 0.73 (0.66-0.81) | <0.001 | 0.80 (0.72-0.89) | <0.001 | 0.83 (0.75-0.92) | 0.001 |

Abbreviations: nPCR, normalized protein catabolic rate; MICS, malnutrition-inflammation cachexia syndrome

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Appendix-Table S3. Association between Change in $n P C R_{\text {dial }+ \text { renal }}$ during first six months and Serum albumin level at $\mathrm{PQ} 3 \geq 3.8$ $\mathrm{g} / \mathrm{dL}$ in 13,882 incident patients

| Likelihood of Serum $\mathrm{Alb} \geq 3.8$ at PQ 3 | Baseline $n P C R_{\text {dial }+ \text { renal }}$ and Baseline Alb adjusted |  | Baseline nPCR ${ }_{\text {dial }+ \text { renal }}$, Baseline Alb, and Case-mix adjusted |  | Baseline nPCR ${ }_{\text {dial }+ \text { renal }}$, Baseline Alb, Case-mix and MICS adjusted |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Change in $\mathrm{nPCR}_{\text {dial + renal }}$ (g/kg/day) | Odds Ratio (95\% confidence interval) | $P$ value | Odds Ratio (95\% confidence interval) | $P$ value | Odds Ratio (95\% confidence interval) | $P$ value |
| $<-0.2$ | 0.49 (0.42-0.58) | <0.001 | 0.48 (0.41-0.57) | <0.001 | 0.53 (0.44-0.63) | <0.001 |
| $-0.2 \leq$ and $<-0.1$ | 0.61 (0.51-0.73) | <0.001 | 0.59 (0.50-0.71) | <0.001 | 0.62 (0.51-0.74) | <0.001 |
| $-0.1 \leq$ and $<0$ | 0.75 (0.64-0.88) | <0.001 | 0.75 (0.64-0.88) | <0.001 | 0.77 (0.66-0.91) | 0.002 |
| $0 \leq$ and $<0.1$ | 0.92 (0.79-1.07) | 0.30 | 0.92 (0.79-1.07) | 0.28 | 0.94 (0.80-1.10) | 0.43 |
| $0.1 \leq$ and $<0.2$ | 1.00 | NA | 1.00 | NA | 1.00 | NA |
| $0.2 \leq$ and $<0.3$ | 1.27 (1.08-1.48) | 0.004 | 1.27 (1.08-1.49) | 0.004 | 1.26 (1.07-1.48) | 0.006 |
| $0.3 \leq$ and $<0.4$ | 1.28 (1.07-1.53) | 0.006 | 1.30 (1.09-1.56) | 0.004 | 1.30 (1.08-1.56) | 0.005 |
| $0.4 \leq$ and $<0.5$ | 1.56 (1.27-1.90) | <0.001 | 1.54 (1.26-1.89) | <0.001 | 1.55 (1.26-1.90) | <0.001 |
| $0.5 \leq$ | 1.58 (1.32-1.90) | <0.001 | 1.59 (1.32-1.92) | <0.001 | 1.62 (1.35-1.96) | <0.001 |

Abbreviations: Alb, albumin; nPCR, normalized protein catabolic rate; MICS, malnutrition-inflammation cachexia syndrome

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Appendix-Table S4. Association between change in nPCR dial $^{\text {renal }}$ and 4.5-year mortality in 13,895 incident patients

| All-cause mortality | Baseline $\mathrm{nPCR}_{\text {dial + renal }}$ adjusted |  | Baseline nPCR ${ }_{\text {dial+renal }}$ and case-mix adjusted |  | Baseline nPCR ${ }_{\text {dial }+ \text { renal }}$, case-mix and MICS adjusted |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Change in $n^{n P C R}$ dial +renal (g/kg/day) | Hazard Ratio (95\% confidence interval) | $P$ value | Hazard Ratio (95\% confidence interval) | $P$ value | Hazard Ratio (95\% confidence interval) | $P$ value |
| $\leq-0.2$ | 1.43 (1.23-1.66) | $<0.001$ | 1.47 (1.27-1.71) | <0.001 | 1.32 (1.14-1.54) | <0.001 |
| $>-0.2$ and $\leq-0.1$ | 1.22 (1.05-1.42) | 0.01 | 1.29 (1.10-1.50) | 0.001 | 1.22 (1.04-1.42) | 0.01 |
| $>-0.1$ and $\leq 0$ | 1.10 (0.96-1.26) | 0.18 | 1.12 (0.98-1.28) | 0.11 | 1.11 (0.97-1.27) | 0.14 |
| $>0$ and $\leq 0.1$ | 1.00 (0.88-1.15) | 0.98 | 1.02 (0.89-1.17) | 0.75 | 1.01 (0.88-1.15) | 0.91 |
| $>0.1$ and $\leq 0.2$ | 1.00 | NA | 1.00 | NA | 1.00 | NA |
| $>0.2$ and $\leq 0.3$ | 0.93 (0.81-1.07) | 0.31 | 0.93 (0.81-1.08) | 0.35 | 0.89 (0.77-1.02) | 0.1 |
| $>0.3$ and $\leq 0.4$ | 0.93 (0.80-1.09) | 0.40 | 0.90 (0.77-1.05) | 0.20 | 0.86 (0.74-1.01) | 0.07 |
| $>0.4$ and $\leq 0.5$ | 0.91 (0.77-1.09) | 0.31 | 0.89 (0.75-1.06) | 0.19 | 0.82 (0.69-0.97) | 0.02 |
| $0.5<$ | 0.86 (0.73-1.02) | 0.08 | 0.82 (0.70-0.97) | 0.02 | 0.76 (0.64-0.90) | 0.001 |

Abbreviations: nPCR, normalized protein catabolic rate; MICS, malnutrition-inflammation cachexia syndrome

## Appendix-Figure S1.



## Appendix-Figure S2.



B


