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## Supplemental Appendix. Causal Mediation Analysis Interpretation

The association of eGFR with gait speed (the total effect (TE)) is decomposed into two parts: (1) the component that works through a gait marker; the gait marker is in the causal pathway between eGFR and gait speed, and is therefore a mediator of the effect – this is called the natural indirect effect (NIE); and (2) the component that does not work through the gait marker – the controlled direct effect (CDE). The magnitude of mediation is often expressed as the proportion mediated, calculated as NIE/TE. However, when the NIE and CDE are in opposite directions – as in this case – the proportion mediated may be >100% and thus is not a meaningful calculation. Nevertheless, the observation that the NIE is of nearly the same magnitude as the TE for three of the gait markers indicates that mediation by these markers completely, or nearly completely, accounts for the association of eGFR with gait speed. In contrast, stride length variability and cadence have significant CDEs, and these are of similar magnitude to the TE: therefore, the eGFR-gait speed association is not mediated by these gait markers.

**Supplemental Table 1. Characteristics at Enrollment Visit in Participants with and without Blood Samples**

| | No Labs (n=236) | Labs (n=350) |
|---|---|---|
| Age (yrs) | 77.1 ± 6.7 | 76.5 ± 6.5 |
| Women – n(%) | 136 (58) | 189 (54) |
| Race – n(%) (n=584) | | |
| *White* | 199 (85) | 274 (79) |
| *Black* | 33 (14) | 66 (19) |
| *Other* | 3 (1) | 9 (3) |
| Comorbidities (global health score) – n(%) (n=545) | | |
| *0* | 36 (18) | 51 (15) |
| *1* | 62 (31) | 102 (29) |
| *2* | 62 (31) | 119 (34) |
| *3+* | 38 (19) | 75 (22) |
| Gait speed (cm/s) (n=584) | 96.5 ± 21.0 | 98.6 ± 23.7 |

**Supplemental Table 2. Associations of continuous eGFR* with quantitative gait markers after adjustment for medications or exclusion of diabetes or neuropathy**

Additional adjustment for medication count†

| | eGFR ≥ 60 (N=196) | | eGFR<60 (N=134) | |
|---|---|---|---|---|
| **Gait Marker** | Coefficient | p value | Coefficient | p value |
| Speed (cm/s) | 0.03 (-2.5 to 2.6) | 0.98 | 3.2 (0.5 to 5.8) | 0.02 |
| Stride length (cm) | -0.5 (-2.6 to 1.5) | 0.62 | 3.5 (1.3 to 5.7) | 0.002 |
| Swing (%) | -0.2 (-0.5 to 0.1) | 0.31 | 0.7 (0.3 to 1.0) | <0.001 |
| Double support (%) | 0.2 (-0.4 to 0.7) | 0.59 | -1.0 (-1.6 to -0.4) | 0.001 |
| Stride length variability (SD) | -0.1 (-0.3 to 0.1) | 0.44 | 0.1 (-0.2 to 0.3) | 0.68 |
| Cadence (steps/min) | 0.5 (-1.0 to 1.9) | 0.53 | 0.3 (-1.2 to 1.8) | 0.73 |

Excluding participants with diabetes†

| | eGFR ≥ 60 (N=160) | | eGFR<60 (N=105) | |
|---|---|---|---|---|
| **Gait Marker** | Coefficient | p value | Coefficient | p value |
| Speed (cm/s) | -0.9 (-3.8 to 2.0) | 0.55 | 2.7 (-0.3 to 5.7) | 0.08 |
| Stride length (cm) | -1.5 (-3.8 to 0.8) | 0.21 | 3.2 (0.7 to 5.6) | 0.01 |
| Swing (%) | -0.3 (-0.7 to 0.03) | 0.07 | 0.6 (0.3 to 1.0) | 0.001 |
| Double support (%) | 0.2 (-0.4 to 0.8) | 0.52 | -0.8 (-1.5 to -0.2) | 0.01 |
| Stride length variability (SD) | -0.1 (-0.3 to 0.2) | 0.68 | -0.04 (-0.3 to 0.2) | 0.75 |
| Cadence (steps/min) | 0.3 (-1.3 to 1.9) | 0.74 | 0.2 (-1.5 to 1.9) | 0.83 |

Excluding participants with a history of neuropathy†

| | eGFR ≥ 60 (N=174) | | eGFR<60 (N=119) | |
|---|---|---|---|---|
| **Gait Marker** | Coefficient | p value | Coefficient | p value |
| Speed (cm/s) | -1.0 (-3.8 to 1.7) | 0.47 | 3.3 (0.4 to 6.2) | 0.02 |
| Stride length (cm) | -1.3 (-3.5 to 0.9) | 0.26 | 3.4 (1.1 to 5.7) | 0.004 |
| Swing (%) | -0.3 (-0.6 to 0.1) | 0.13 | 0.7 (0.3 to 1.0) | <0.001 |
| Double support (%) | 0.2 (-0.4 to 0.9) | 0.47 | -1.0 (-1.6 to -0.3) | 0.005 |
| Stride length variability (SD) | -0.1 (-0.3 to 0.2) | 0.63 | 0.1 (-0.2 to 0.4) | 0.45 |
| Cadence (steps/min) | -0.1 (-1.6 to 1.5) | 0.94 | 0.6 (-1.0 to 2.2) | 0.47 |

Abbreviations: eGFR, estimated glomerular filtration rate; SD, standard deviation.

* Linear splines for eGFR constructed with knot placed at 60 mL/min/1.73m$^2$

† Models adjusted for age, sex, race, education, body-mass index, self-reported neuropathy, and number of comorbidities

**Supplemental Table 3. Clinical Gait Abnormalities by CKD Status**

| **Characteristic** | No CKD (n=179) | CKD (n=127) | p Value |
|---|---|---|---|
| Marked sway – n(%) | 62 (35) | 66 (52) | 0.002 |
| Lost balance – n(%) | 47 (26) | 55 (43) | 0.002 |
| Wide – n(%) | 17 (10) | 16 (13) | 0.39 |
| Foot drop/drag – n(%) | 11 (6) | 9 (7) | 0.74 |
| Short steps – n(%) | 20 (11) | 35 (28) | <0.001 |
| Shuffling/Difficulty lifting feet – n(%) | 12 (7) | 17 (13) | 0.05 |
| Festination – n(%) | 0 (0) | 0 (0) | n/a |

Abbreviations: CKD, chronic kidney disease. CKD defined as estimated glomerular filtration rate <60 mL/min/1.73m$^2$.
Clinical gait examination data were available for 306 participants. Marked sway and lost balance were defined as positive if present during straight or tandem walking.

**Supplemental Table 4. Associations of Clinical Gait Phenotype and CKD Status with Quantitative Gait Markers***

| | Speed (cm/s) | Stride length (cm) | Swing (%) | Double support (%) | Stride length variability (SD) | Cadence (steps/min) |
|---|---|---|---|---|---|---|
| No CKD, no gait phenotype (n=99) | Ref | Ref | Ref | Ref | Ref | Ref |
| CKD, no gait phenotype (n=40) | -1.1 (-8.8 to 6.6) | 0.3 (-6.1 to 6.7) | -0.3 (-1.2 to 0.7) | 0.7 (-1.1 to 2.5) | -0.5 (-1.2 to 0.2) | -1.3 (-5.7 to 3.0) |
| No CKD, + gait phenotype (n=80) | -7.3 (-13.5 to -1.2) | -5.0 (-10.1 to 0.1) | -0.3 (-1.1 to 0.5) | 1.2 (-0.2 to 2.6) | 0.3 (-0.3 to 0.9) | -2.8 (-6.3 to 0.7) |
| CKD, + gait phenotype (n=87) | -11.1 (-17.8 to -4.4) | -9.4 (-15.0 to -3.8) | -1.1 (-1.9 to -0.2) | 1.9 (0.4 to 3.5) | 0.2 (-0.4 to 0.9) | -3.1 (-6.9 to 0.7) |
| P for trend | <0.001 | 0.001 | 0.03 | 0.01 | 0.22 | 0.07 |

Abbreviations: CKD, chronic kidney disease.

* CKD defined as estimated glomerular filtration rate <60 mL/min/1.73m$^2$. Gait phenotype defined as the presence of short steps or marked sway or loss of balance with straight or tandem walking.

Coefficients calculated using linear regression models adjusted for age, sex, race, education, body-mass index, neuropathy, medication count, and number of comorbidities.

**Supplemental Table 5. Odds Ratio for CKD by gait severity score**

| Gait Severity Score | OR (95% CI) |
|---|---|
| 0 (n=139) | Ref |
| 1 (n=138) | 1.48 (0.84-2.59) |
| 2 (n=29) | 5.25 (1.83-15.04) |
| P for trend | 0.004 |

Abbreviations: CKD, chronic kidney disease; OR, odds ratio; CI, confidence interval

* CKD defined as estimated glomerular filtration rate <60 mL/min/1.73m$^2$. Gait severity score defined as the number of gait abnormalities on clinical gait exam (short steps, marked sway/loss of balance with straight or tandem walking).

Odds ratios calculated using logistic regression models adjusted for age, sex, race, education, body-mass index, neuropathy, medication count, and number of comorbidities.

**Supplemental Table 6. Risk of Falling by Gait Severity Score and CKD Status***

| | | HR (95% CI) | |
|---|---|---|---|
| Gait Severity Score | # of Events | No CKD (n=171) | CKD (n=123) |
| 0 (n=139) | 64 | Ref | Ref |
| 1 (n=138) | 73 | 0.92 (0.56-1.52) | 3.55 (1.69-7.49) |
| 2 (n=29) | 17 | 0.80 (0.18-3.51) | 5.88 (2.12-16.28) |
| P for trend | | 0.69 | <0.001 |

Abbreviations: CKD, chronic kidney disease; HR, hazard ratio; CI, confidence interval

* P-value for interaction of CKD status and gait severity score=0.03. CKD defined as eGFR <60 mL/min/1.73m$^2$. Gait severity score defined as the number of gait abnormalities on clinical gait exam (short steps, marked sway/loss of balance with straight or tandem walking).

Models adjusted for age, sex, race, body-mass index, neuropathy, medication count, number of comorbidities, history of falling, gait speed, and stratified by educational status

**Supplemental Table 7. Risk of Falling by Gait Characteristic and CKD Status***

| | HR (95% CI) | |
|---|---|---|
| **Gait characteristic** | No CKD (n=171) | CKD (n=123) |
| Short steps | 0.41 (0.14-1.19) | 1.87 (0.99-3.56) |
| Marked sway or lost balance | 1.10 (0.68-1.78) | 2.92 (1.55-5.50) |

Abbreviations: CKD, chronic kidney disease; HR, hazard ratio; CI, confidence interval

* P-value for interaction of CKD status and short steps=0.01. CKD defined as eGFR <60 mL/min/1.73m$^2$. Gait characteristic based on clinical gait exam (short steps, marked sway or loss of balance with straight or tandem walking).

Models adjusted for age, sex, race, body-mass index, neuropathy, medication count, number of comorbidities, history of falling, gait speed, and stratified by educational status