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TransplantLines Investigators

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Central Body Fat Distribution and Kidney Function after Living Kidney Donation

Lisa B. Westenberg, Robert A. Pol, Jessica van der Weijden, Martin H. de Borst, Stephan J.L. Bakker, and Marco van Londen, on behalf of the Transplant Lines Investigators*

Abstract

Background In most screening guidelines, high body mass index (BMI) is considered a contraindication for kidney donation. New insights suggest that central body fat distribution might provide greater power in assessing kidney risk. This study aimed to determine whether BMI and central body fat distribution measures are associated with long-term kidney function after donor nephrectomy. We hypothesized that higher BMI, waist circumference (WC), and waist-to-height ratio (WHtR) were associated with lower kidney function long term after donation.

Methods The study population consisted of living kidney donors. BMI, WC, and WHtR were measured during donor screening. The outcome postdonation kidney function was assessed using measured GFR (mGFR, $^{125I}$-iothalamate infusion) at 3 months ($n=1042$), 5 years ($n=556$), and 10 years ($n=210$) of follow-up. Primary multivariable linear regression analyses were performed with BMI and WC and secondary analyses with WHtR. Linear mixed models were performed to investigate change in postdonation eGFR.

Results The donor age was 52±11 years, and 48% were male. The mean BMI was 26.1±3.6 kg/m², and WC was 91±11 cm. Higher predonation BMI was associated with lower mGFR throughout follow-up: $-1.35$ (95% confidence interval [CI], $-1.95$ to $-0.80$), $-1.55$ (95% CI, $-2.50$ to $-0.65$), and $-2.35$ (95% CI, $-4.10$ to $-0.60$) ml/min per m² per 5 kg/m² higher BMI at 3 months, 5, and 10 years after donation, respectively, adjusted for sex, and predonation GFR. For WC, differences in mGFR were $-1.30$ (95% CI, $-1.70$ to $-0.90$), $-1.50$ (95% CI, $-2.20$ to $-0.80$), and $-1.70$ (95% CI, $-3.00$ to $-0.50$) ml/min per m² per 10 cm higher WC at 3 months, 5, and 10 years after donation, respectively. In male donors, BMI and WC were significantly associated with a negative postdonation change in eGFR.

Conclusions Higher BMI and WC were independently associated with lower GFR (long term) after living kidney donation.

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Introduction

Living donor kidney transplantation is the best treatment for kidney failure. Although the absolute risk is low, living donors have a higher risk of kidney failure. To optimize donor screening and care, it is important to identify donors who are at risk of adverse outcomes after donation. Assessing postdonation kidney outcomes in relation to body composition may provide the opportunity to intervene and adjust a suboptimal body composition in preparation for donation.

In the general population, obesity is a potent risk factor for the development of kidney disease. Body mass index (BMI) continues to play an important role in the assessment of a potential donor but has limitations in the accurate measurement of body composition. The distribution pattern of body fat seems to be a more important determinant of kidney hemodynamics than overall weight excess. Central body fat distribution has been associated with lower GFR and higher filtration fraction in prospective living kidney donors, independent of BMI. It has also been associated with greater risk of microalbuminuria and diminished filtration, even in lean individuals. Therefore, measuring central fat distribution might be beneficial in predonation risk assessment of potential kidney donors. Various methods, such as waist circumference (WC), waist-to-hip ratio, and waist-to-height ratio (WHtR), measure central fat distribution. WC correlates strongly with radiological measurements of abdominal adiposity. Waist-to-hip ratio may not be helpful in practice because
with weight reduction both waist and hip circumference can decrease, changing the ratio very little. WHR offers an alternative, possibly reducing overestimation or underestimation of risk in tall and short individuals with similar WC.\textsuperscript{15} WHtR is associated with the risk of cardiovascular disease, diabetes, and obesity-related CKD.\textsuperscript{15–17}

The association between a central fat distribution and kidney function after living kidney donation is unknown. This study aimed to determine whether BMI and central body fat distribution measures are associated with kidney function after donor nephrectomy in a group of donors with relatively normal body sizes. We hypothesized that a higher BMI, WC, and WHtR are associated with lower kidney function after donation.

**Methods**

**Study Design**

A total of 1042 living kidney donors were included in this longitudinal cohort study. All donor nephrectomies took place between 1980 and 2018 in the University Medical Center Groningen. The main inclusion criterion for the study was age 18 years or older. Exclusion criteria for donation were in accordance with the Dutch Guidelines for Evaluation of Potential Donors for Living Donor Kidney Transplantation (i.e., BMI \(\geq 35\) kg/m\(^2\), unable to provide informed consent, manifested diabetes mellitus, major cardiovascular risk factors, prior kidney disease or GFR <60 ml/min per 1.73 m\(^2\), monokidney, pregnancy, recent or active malignancies, chronic/active infection [e.g., human immunodeficiency virus, hepatitis C virus, human T-lymphotropic virus, hepatitis B virus], hypertension with end organ damage, inadequately regulated hypertension, proteinuria \(>0.5\) g/24 hours), microscopical hematuria, and bilateral nephrolithiasis on computed tomography scan). An overview of the participants and available data is displayed in Figure 1.

**Data Collection**

All data were retrieved from the TransplantLines Biobank and Cohort Study (ClinicalTrials.gov identifier: NCT03272841). This is an ongoing, prospective study aiming to assess short-term and long-term outcomes after solid organ transplantation and donation. All participants gave written informed consent on enrollment. A detailed

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![Figure 1. Overview of the participants and available data. Dotted line: data not included in this study. COVID-19, coronavirus disease 2019; mGFR, measured GFR. Figure 1 can be viewed in color online at www.cjasn.org.](image-url)
description of the study design and inclusion and exclusion criteria has been described previously. The study protocol has been approved by the local Institutional Review Board (METc 2014/077), adheres to the University Medical Center Groningen Biobank Regulation, and is in accordance with the World Medical Association’s Declaration of Helsinki. The clinical and research activities being reported are consistent with the Principles of the Declaration of Istanbul as outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism. Measurements were performed at four time points: as part of the screening process before donor nephrectomy and after donor nephrectomy at 3 months, 5 years, and 10 years of follow-up. eGFR was also determined at additional time points after donation.

**Measurements and Calculations**

BMI was calculated as weight (kg)/height$^2$ (m$^2$), and WHtR was calculated as WC (cm)/height (cm). Kidney function was expressed as measured GFR (mGFR), using $^{125}$I-iothalamate infusion in accordance with the procedure described in a previous study by our group. We present mGFR values that are indexed for the donor’s body surface area (BSA) (ml/min per m$^2$), which is a common practice in the literature. For the linear mixed models, kidney function was primarily assessed using eGFR because there were more repeated measurements of eGFR after donation than mGFR. eGFR was calculated following the CKD Epidemiology Collaboration 2021 creatinine equation. All other biochemical measurements were performed as described previously.

**Statistical Analysis**

Data were analyzed using SPSS version 28.0 (IBM, Armonk) and RStudio (PBC, Boston, MA, 2021). Normality was evaluated with histograms and quantile–quantile plots. Normally distributed variables are presented as mean (SD). To determine which body measures are associated with kidney function, unadjusted and adjusted linear regression analyses were performed. Primary linear regression analyses were performed with BMI and WC. Secondary linear regression analyses were performed with WHtR. GFR after kidney donation is influenced by age, sex, and predonation GFR. Age and mGFR at screening for donation both had a quadratic relationship with mGFR levels after donation. Therefore, quadratic terms of age and predonation mGFR were added to our multivariable regression model (age$^2$ and age$^2$×mGFR, respectively). All analyses were performed for the total study population and for male and female donors separately. Linear mixed models adjusted for age and age squared were used to assess the association between anthropometric measurements at screening (independent variable) and changes in eGFR and mGFR after donation (dependent variable). Data from donors who were lost to follow-up were not included in the regression analyses at the time point(s) for which these donors did not have mGFR data. Multiple imputation, using the fully conditional specification method, was undertaken at each time point for all covariables containing missing data in the linear regression analyses. Two-tailed $P$ values were used, and significance was set at $P < 0.05$. Homoscedasticity and normal distribution of residuals were present in all models. The Durbin–Watson test was used to check autocorrelation of residuals.

**Results**

A total of 1042 donors had mGFR data at 3 months, 556 at 5 years, and 210 at 10 years after donation. The results of a missing value analysis are presented in Supplemental Table 1. Extent and reasons for loss to follow-up at each time point after donation are displayed in Figure 1. Of all donors, 48% were male (Table 1). The age at the time of screening was 52±11 years, and BMI was 26.1±3.6 kg/m$^2$. WC was 88±10 cm in female and 95±10 cm in male donors, and WHtR was 0.52±0.06 in both female and male donors. mGFR at screening was 114±22 ml/min. Unadjusted and age-adjusted linear regression analyses of BMI, WC, and WHtR with baseline mGFR as dependent variable

<table>
<thead>
<tr>
<th>Table 1. Baseline characteristics of living kidney donors included in this study who donated between 1980 and 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor characteristic</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>No.</td>
</tr>
<tr>
<td>Age at screening, yr</td>
</tr>
<tr>
<td>Weight, kg</td>
</tr>
<tr>
<td>Height, cm</td>
</tr>
<tr>
<td>BMI, kg/m$^2$</td>
</tr>
<tr>
<td>BSA, m$^2$</td>
</tr>
<tr>
<td>Hip circumference, cm</td>
</tr>
<tr>
<td>WC, cm</td>
</tr>
<tr>
<td>WHtR</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
</tr>
<tr>
<td>mGFR, ml/min</td>
</tr>
<tr>
<td>Urinary creatinine excretion, mg/24 h</td>
</tr>
</tbody>
</table>

BMI, body mass index (kg/m$^2$); BSA, body surface area (m$^2$); mGFR, measured GFR (ml/min); WC, waist circumference; WHtR, waist-to-height ratio.

Values are given as No. (%) or mean±SD.
showed a significant negative association between BMI and kidney function in female donors (Supplemental Table 2).

**Anthropometrics and Kidney Function after Donation**

In unadjusted linear regression analyses, BMI was not significantly associated with postdonation eGFR (Table 2). Adjusting for sex, age, and predonation mGFR uncovered a negative association between BMI and mGFR at all time points after donation in the total study population. Higher predonation BMI was associated with lower mGFR throughout follow-up: $-1.35 \text{ ml/min per m}^2$ at 3 months ($P < 0.001$), $-1.55 \text{ ml/min per m}^2$ at 5 years ($P < 0.001$), and $-2.35 \text{ ml/min per m}^2$ at 10 years ($P = 0.01$), per 5 kg/m$^2$ higher BMI (Table 2). Interaction effects of sex with the body measure were not statistically significant. When performing these analyses for male and female donors separately, the associations between BMI and postdonation kidney function remained significant at all time points for male donors and at 3 months and 5 years after donation for female donors.

In unadjusted analyses, WC was associated with mGFR at 3 months after donation in the total study population (Table 3). Linear regression analyses that were adjusted for sex, age, and predonation mGFR showed that in the total study population higher WC was significantly associated with lower mGFR at all time points after donation. Per 10 cm larger WC, differences in mGFR were $-1.30 \text{ ml/min per m}^2$ at 3 months postdonation ($P < 0.001$), $-1.50 \text{ ml/min per m}^2$ at 5 years ($P < 0.001$), and $-1.70 \text{ ml/min per m}^2$ at 10 years ($P = 0.01$) (Table 3). Interaction effects of sex with the body measure were not statistically significant. In male donors, WC was significantly associated with lower kidney function at all time points after donation in analyses adjusted for age and predonation GFR. In female donors, these associations were significant at 3 months and 5 years after donation.

In secondary unadjusted analyses, WHtR was associated with mGFR at 3 months and 5 years after donation in the total study population (Table 4). After adjusting for sex, age, and predonation mGFR, these associations were significant at all time points after donation. Per 1 cm/cm higher WHtR, differences in mGFR were $-11.5 \text{ ml/min per m}^2$ at 3 months ($P = 0.002$), $-19.4 \text{ ml/min per m}^2$ at 5 years ($P = 0.002$), and $-25.6 \text{ ml/min per m}^2$ at 10 years ($P = 0.03$) (Table 4). In male donors, higher WHtR was significantly associated with lower postdonation kidney function at all time points. In female donors, this association was significant at 3-month follow-up and borderline nonsignificant at 5-year follow-up.

Figure 2 illustrates the differences in postdonation kidney function per unit of anthropometric measurements.

**Analysis of Body Composition Measurements and Change in Postdonation Kidney Function**

Linear mixed models adjusted for age and age squared were performed with body composition measurements at screening and postdonation eGFR. The median follow-up of eGFR after donation was 7 (5–11) years. Linear mixed models showed a significant association with negative annual postdonation eGFR change for BMI, WC, and WHtR in male living kidney donors (per 5 kg/m$^2$ higher BMI: $-0.40 \text{ ml/min per m}^2$, $P < 0.001$; per 10 cm higher WC: $-0.20 \text{ ml/min per m}^2$, $P = 0.001$; per 1 cm/cm higher WHtR: $-3.64 \text{ ml/min per m}^2$, $P = 0.004$) (Supplemental Table 3). In female donors, no body composition measures were significantly associated with postdonation eGFR in linear mixed model analyses. The association between BMI and postdonation change in eGFR was borderline statistically nonsignificant in female donors. In analyses with postdonation mGFR in male donors, higher BMI and WHtR were significantly associated with a negative monthly change in postdonation mGFR (per 5 kg/m$^2$ higher BMI: $-0.02 \text{ ml/min per m}^2$, $P = 0.01$; per 1 cm/cm higher WHtR: $-0.18 \text{ ml/min per m}^2$, $P = 0.02$) (Supplemental Table 4). WC in male donors was not significantly associated with postdonation change in mGFR, although it was borderline nonsignificant. In female donors, no anthropometric measurements were significantly associated with postdonation change in mGFR.

**Discussion**

We had hypothesized that a higher BMI, WC, and WHtR are associated with lower kidney function after donation. This study shows that in living kidney donors with relatively normal body sizes, BMI, WC, and WHtR were significantly associated with kidney function after donation. This suggests a detrimental role of an unfavorable predonation body composition (i.e., higher BMI and central body fat distribution) on kidney outcomes after living kidney donation.

Previous studies in nondonor populations show a somewhat comparable relationship between BMI and kidney function impairment, with a higher risk of kidney disease. In living kidney donors, studies on the effect of BMI on long-term kidney function after donation show contradictory findings with both significant and nonsignificant (adverse) effects on kidney function short term or long term after donation. Although BMI is a widely used measure of excess weight, it becomes clearer that the distribution pattern of excess weight plays a more important role in kidney dynamics. The results of this study showed a significant association between higher WC and WHtR during screening for donation and lower GFR levels after donation. Although cross-sectional studies have previously reported an association between central body fat distribution and unfavorable kidney hemodynamics in the nondiabetic general population and prospective living kidney donors (e.g., lower GFR, lower effective kidney plasma flow, and higher filtration fraction). Our results show that this relationship also exists after kidney donation.

The association of central fat distribution with kidney hemodynamics is often ascribed to associated cardiometabolic risk factors, such as hypertension, dyslipidemia, and insulin resistance. Greater insulin and glucagon levels were found in individuals with central fat distribution in comparison with those with a peripheral fat distribution. Insulin and glucagon are presumed to affect kidney hemodynamics and subsequently influence GFR and albuminuria. Furthermore, mechanisms in which proinflammatory adipokines and cytokines are upregulated, causing oxidative stress and inflammation, may...
Table 2. Associations of body mass index at screening with measured GFR after living kidney donation

<table>
<thead>
<tr>
<th>BMI Unadjusted</th>
<th>Sex-Adjusted and Age-Adjusted</th>
<th>Sex-Adjusted, Age-Adjusted, and Baseline GFR-Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Difference in mGFR/BSA (95% CI), ml/min per m² per 5 kg/m² BMI</td>
<td>P Value</td>
</tr>
<tr>
<td>All Donors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 mo, n=1042</td>
<td>−0.40 (−0.95 to 0.15)</td>
<td>0.14</td>
</tr>
<tr>
<td>5 yr, n=556</td>
<td>−0.60 (−1.40 to 0.20)</td>
<td>0.13</td>
</tr>
<tr>
<td>10 yr, n=210</td>
<td>−0.40 (−1.80 to 1.00)</td>
<td>0.56</td>
</tr>
<tr>
<td>Male Donors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 mo, n=505</td>
<td>−0.15 (−0.95 to 0.65)</td>
<td>0.71</td>
</tr>
<tr>
<td>5 yr, n=254</td>
<td>−0.95 (−2.25 to 0.35)</td>
<td>0.14</td>
</tr>
<tr>
<td>10 yr, n=102</td>
<td>−1.85 (−4.35 to 0.7)</td>
<td>0.16</td>
</tr>
<tr>
<td>Female Donors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 mo, n=537</td>
<td>−0.70 (−1.40 to 0.05)</td>
<td>0.07</td>
</tr>
<tr>
<td>5 yr, n=302</td>
<td>−0.55 (−1.60 to 0.45)</td>
<td>0.28</td>
</tr>
<tr>
<td>10 yr, n=108</td>
<td>0.80 (−0.80 to 2.45)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

BMI, body mass index (kg/m²); BSA, body surface area (m²); CI, confidence interval; mGFR, measured GFR (ml/min per BSA).

Model 1: body mass index; model 2: model 1 + age at screening (years) + age at screening (years)² + sex + body mass index × sex, in model with all donors; model 3: model 2 + pre-donation mGFR (ml/min) + pre-donation mGFR (ml/min)².

a P value interaction sex × body mass index model 2, 3 months = 0.05.
b P value interaction sex × body mass index model 3, 3 months = 0.30.
c P value interaction sex × body mass index model 3, 5 years = 0.21.
d P value interaction sex × body mass index model 3, 10 years = 0.52.
e P value interaction sex × body mass index model 3, 10 years = 0.31.
Table 3. Associations of waist circumference at screening with measured GFR after living kidney donation

<table>
<thead>
<tr>
<th>WC</th>
<th>Unadjusted</th>
<th>Sex-Adjusted and Age-Adjusted</th>
<th>Sex-Adjusted, Age-Adjusted, and Baseline GFR-Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Difference in mGFR/BSA (95% CI), ml/min per m² per 10 cm WC</td>
<td>Difference in mGFR/BSA (95% CI), ml/min per m² per 10 cm WC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P Value</td>
<td>P Value</td>
</tr>
<tr>
<td>All Donors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 mo, n=1042</td>
<td></td>
<td>-0.50 (-0.80 to -0.10)</td>
<td>0.01</td>
</tr>
<tr>
<td>5 yr, n=556</td>
<td>-0.30 (-1.00 to 0.30)</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>10 yr, n=210</td>
<td>-0.20 (-1.20 to 0.70)</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Donors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 mo, n=505</td>
<td>-0.60 (-1.10 to -0.01)</td>
<td>0.045</td>
<td></td>
</tr>
<tr>
<td>5 yr, n=254</td>
<td>-1.40 (-2.40 to -0.40)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>10 yr, n=102</td>
<td>-1.30 (-3.00 to 0.50)</td>
<td>0.17</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Female Donors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 mo, n=537</td>
<td>-0.70 (-1.20 to -0.10)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>5 yr, n=302</td>
<td>-0.10 (-0.90 to 0.70)</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td>10 yr, n=108</td>
<td>0.90 (-0.50 to 2.40)</td>
<td>0.21</td>
<td></td>
</tr>
</tbody>
</table>

BSA, body surface area (m²); CI, confidence interval; mGFR, measured GFR (ml/min per BSA); WC, waist circumference (cm).
Model 1: waist circumference; model 2: model 1 + age at screening (years) + sex at screening (years)² (× sex + waist circumference × sex, in model with all donors); model 3: model 2 + predonation mGFR (ml/min) + predonation mGFR (ml/min).²

*P value interaction sex × waist circumference model 2, 3 months = 0.09.
*P value interaction sex × waist circumference model 3, 3 months = 0.52.
*P value interaction sex × waist circumference model 2, 5 years = 0.70.
*P value interaction sex × waist circumference model 3, 5 years = 0.22.
*P value interaction sex × waist circumference model 2, 10 years = 0.19.
*P value interaction sex × waist circumference model 3, 10 years = 0.06.
Table 4. Associations of waist-to-height ratio at screening with measured GFR after living kidney donation

<table>
<thead>
<tr>
<th>WHtR</th>
<th>Unadjusted</th>
<th>Sex-Adjusted and Age-Adjusted</th>
<th>Sex-Adjusted, Age-Adjusted, and Baseline GFR-Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Difference in mGFR/BSA (95% CI), ml/min per m² per 1 cm/cm WHtR</td>
<td>P Value</td>
<td>Difference in mGFR/BSA (95% CI), ml/min per m² per 1 cm/cm WHtR</td>
</tr>
<tr>
<td>All Donors</td>
<td>3 mo, n=1042</td>
<td>-10.4 (-17.1 to -3.65)</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>5 yr, n=556</td>
<td>-14.2 (-26.0 to -2.47)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>10 yr, n=210</td>
<td>-9.74 (-27.9 to 8.45)</td>
<td>0.29</td>
</tr>
<tr>
<td>Male Donors</td>
<td>3 mo, n=505</td>
<td>-10.6 (-20.5 to 0.71)</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>5 yr, n=254</td>
<td>-31.6 (-49.5 to -13.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>10 yr, n=102</td>
<td>-38.0 (-70.3 to -5.68)</td>
<td>0.02</td>
</tr>
<tr>
<td>Female Donors</td>
<td>3 mo, n=537</td>
<td>-10.3 (-19.5 to -1.18)</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>5 yr, n=302</td>
<td>-4.01 (-17.4 to 9.43)</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>10 yr, n=108</td>
<td>10.7 (-15.0 to 36.4)</td>
<td>0.40</td>
</tr>
</tbody>
</table>

BSA, body surface area (m²); CI, confidence interval; mGFR, measured GFR (ml/min per BSA); WHtR, waist-to-height ratio.

Model 1: waist-to-height ratio; model 2: model 1 + age at screening (years); model 3: model 2 + predonation mGFR (ml/min) + predonation GFR (ml/min).

*P value interaction sex × waist-to-height ratio model 2, 3 months = 0.08.

†P value interaction sex × waist-to-height ratio model 3, 3 months = 0.26.

‡P value interaction sex × waist-to-height ratio model 2, 5 years = 0.41.

§P value interaction sex × waist-to-height ratio model 3, 5 years = 0.19.

‖P value interaction sex × waist-to-height ratio model 2, 10 years = 0.08.

¶P value interaction sex × waist-to-height ratio model 3, 10 years = 0.07.
underly a direct pathogenic role of weight excess on kidney function.\textsuperscript{33} Future studies are needed to further clarify the pathways by which weight excess and specifically a central fat distribution affect kidney function.

At 10 years postdonation, the negative associations of higher BMI and central fat distribution with kidney function were only present in male living kidney donors. In addition, the linear mixed models only showed significant or borderline nonsignificant associations of BMI, WC, and WHtR with postdonation change in eGFR and mGFR in male donors. The reason for this could lie in differences in body composition between male and female donors at baseline. During screening for donation, male donors had significantly higher levels of BMI and WC. This phenomenon has often been described in the literature, where men are found more likely to develop a central body fat distribution, whereas women more often develop a peripheral fat distribution with fat accumulation in the hip and thigh regions.\textsuperscript{34} Female donors in this study might not have exceeded BMI or WC levels detrimental to kidney function long term after donation. Although our data do not allow differentiation between visceral and subcutaneous fat, it is possible that the distribution of abdominal adipose tissue also plays a role. It is known that men generally have more visceral fat, whereas women have more subcutaneous fat.\textsuperscript{34,35} Especially excess visceral fat,

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**Figure 2. Differences in kidney function per unit of anthropometric measurements.** Results from sex-adjusted, age-adjusted, and pre-donation mGFR-adjusted linear regression analyses in the total study population. (A) Difference in mGFR/BSA at 3 months postdonation, per 5 kg/m$^2$ higher BMI, per 10 cm higher WC, and per 1 cm/cm higher WHtR, with 95% CIs. (B) Difference in mGFR/BSA at 5 years postdonation. (C) Difference in mGFR/BSA at 10 years postdonation. BMI, body mass index (kg/m$^2$); BSA, body surface area (m$^2$); CI, confidence interval; WC, waist circumference; WHtR, waist-to-height ratio.
BMI be addressed. Almost all donors were of European descent, 10 years. This study also has some limitations that need to be addressed. Almost all donors were of European descent, and only 12 participants in this study had a predonation BMI >35 kg/m², hampering generalizability to more ethnically diverse and obese populations. The 12 participants with a BMI >35 kg/m² at initial screening for donation achieved a lower BMI that made these individuals eligible as donors, after which they proceeded to donate. Noteworthy is that a central body fat distribution with high waist-to-hip ratio has been associated with lower GFR and higher filtration fraction, independent of BMI, in prospective living kidney donors.14

The advancement of care for living kidney donors is facilitated by an improved understanding of the relationship between body composition pre-donation and post-donation outcomes. By focusing on body composition, one of the few things that can be modified before donation, we have the opportunity to enhance the outcomes of the donation process. It is crucial to gather evidence supporting the existence of a specific pathological body composition type that is associated with post-donation (kidney) risks. Such evidence is essential for developing strategies to improve predonation body composition, ultimately leading to the optimization of care provided to living kidney donors. This study demonstrates that even in donors with a relatively normal body size, a higher BMI and central fat distribution are associated with lower kidney function after donation. These findings can be used to guide interventions aimed at improving body composition before donation. It would be interesting if future studies could concentrate on determining which specific body composition may have detrimental impact on the outcome of living kidney donation, also taking aspects other than kidney function into account, and possibly establish a cutoff point to help guide the management of (potential) living kidney donors. Consideration should then also be given to factors that affect the connection between body composition and the outcome of donation, such as the onset of (metabolic) comorbidities during the follow-up period.

In conclusion, this study shows that higher BMI, WC, and WHR were significantly associated with lower GFR after living kidney donation. Although the magnitude might seem small, it suggests a detrimental role of predonation central fat distribution on kidney outcomes long-term after donation, and this relationship may be even more pronounced in more obese populations.

Disclosures
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Data Sharing Statement
Partial restrictions to the data and/or materials apply. The data underlying this article will be shared on reasonable request to the corresponding author.

Supplemental Material
This article contains the following supplemental material online at http://links.lww.com/CJN/B851.
Supplemental Table 1. Missing value analysis of variables at screening for donation.
Supplemental Table 2. Linear regression analyses of anthropometric body composition measures with kidney function before donation as dependent variable.
Supplemental Table 3. Longitudinal analysis of tomographic fat indexes and change in eGFR.
Table 4. Longitudinal analysis of tomographic fat indexes and change in mGFR.

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