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Effect of Chronic Dementia Caregiving and Major Transitions in the Caregiving Situation on Kidney Function: A Longitudinal Study

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Abstract

Objective—To estimate the glomerular filtration rate (GFR) in relation to the chronic stress of dementia caregiving and major transitions in the caregiving situation.

Methods—We longitudinally assessed 119 elderly spousal Alzheimer's disease (AD) caregivers and 58 non-caregiving controls for a period of up to three years (mean of 2.8 assessments per participant). Random regression models with fixed and time-variant effects for psychosocial factors, risk factors of chronic kidney disease, and caregiving transitions were used to evaluate changes over time in estimated GFR.

Results—The change in GFR did not differ between caregivers and controls during follow-up ($p=.77$). Further analyses revealed that GFR declined disproportionately following placement of the spouse in a nursing home at 3 months post-placement (−4.9±2.2 mL/min/1.73m2; $p=.03$). Post hoc analyses showed that this effect was stronger in caregivers with hypertension compared to those without hypertension (−5.7±3.1 vs. −2.4±3.4 mL/min), as well as in caregivers with diastolic BP levels at 1 standard deviation above the mean than in those with diastolic BP levels at 1 standard deviation below the mean (−8.3±2.9 vs. −1.4±2.7 mL/min).

Conclusions—Kidney function did not differ between caregivers and controls over time. However, GFR had impaired at 3 months after a major caregiving transition. As the effect of placement of the AD spouse on the decline in GFR was moderated by BP, it might be confined to caregivers who experience increased sympathetic activation post-placement.

Keywords

Blood pressure; caregivers; dementia; kidney disease; psychological stress

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INTRODUCTION

In 2009, almost 11 million family and other unpaid caregivers provided an estimated 12.5 billion hours of care to persons with Alzheimer's disease (AD) and other dementias in the United States (1). These numbers are a public health concern because dementia caregiving takes its toll on caregivers' mental and physical health (2, 3). When compared to their non-caregiving counterparts, AD caregivers have a higher risk of developing incident coronary heart disease (4, 5) and other cardiometabolic alterations (6, 7). AD caregivers' depressed mood and burden shortens the time to a diagnosis of cardiovascular disease (CVD) (8). Immune dysregulation with AD caregiving stress includes proinflammatory changes (9) and accelerated aging of the immune system (10), both of which might help to explain the increased CVD risk in AD caregivers (11).

Chronic psychosocial stress, including low socioeconomic status (SES), and psychological distress might both contribute to a gradual decline in kidney function towards chronic kidney disease (CKD) with a potentially fatal outcome (12). In the Jackson Heart Study, the prevalence of CKD – as defined by a glomerular filtration rate (GFR) below 60 mL/min/1.73 m^2 – was higher in participants with low socioeconomic status (SES) than in those with high SES (13). In longitudinal cohort studies low area SES predicted progression of CKD (14) and clinically elevated depressive symptom levels predicted decline in GFR as well as incident end stage renal disease (15) after several years of follow-up. In hemodialysis patients, poor mental quality of life (16), low social support (17), low dyadic satisfaction (18), and a diagnosis of depression (19) were all prospectively associated with increased mortality.

Impaired kidney function has been associated with an increased CVD risk in the elderly (20), and major risk factors for CKD and CVD are the same, including hypertension, diabetes, obesity, adverse health behaviors, and immune system dysfunction (e.g., elevated circulating levels of proinflammatory cytokines) (12, 21–23). In addition, low hemoglobin levels and previous kidney disease may hasten, while BP- and cholesterol-lowering drugs may slow decline in glomerular function (24, 25). Given that cardiovascular health is poor in AD caregivers, CVD and CKD have a common risk profile, and psychosocial factors seem to contribute to CKD, it is surprising that kidney function has not been examined in relation to the chronic stress of AD caregiving.

We examined the trajectory of GFR as estimated by the Modification of Diet in Renal Disease (MDRD) Study formula in a group of spousal AD caregivers over a period of up to three years and compared it to that of non-caregiving controls while taking into account important covariates of kidney function. Our primary hypothesis was that caregivers have a steeper decline in estimated GFR over time compared to non-caregiving controls, reflecting overall worsening of kidney function in caregivers. Moreover, caregivers are inherently confronted with transitions in the caregiving situation, typically placement of the AD spouse in a nursing home or death of their spouse. Therefore, our second hypothesis was that these two major caregiving transitions would affect caregivers' GFR. Not all caregivers react the same way to both the ongoing situation of providing in-home care and caregiving transitions, either psychologically or biologically (26–28) such that the biobehavioral reaction to the caregiving situation and transitions might differentially affect GFR. Therefore, we expected that GFR would decline over time as well as at 3 months after a transition in those caregivers with increased psychological distress and risk factors for CDK. This may particularly apply to hypertension and elevated blood pressure (BP), respectively as BP increase may lead to a decline in kidney function due to the associated increased glomerular capillary hypertension (25). In prior studies we found AD caregivers developed systemic hypertension at an earlier stage than non-caregiving controls (29) and that placement and death of the AD spouse were both associated with an increased BP response of caregivers to postural challenge (30).

METHODS

Study Participants and Design

The University of California, San Diego (UCSD) Institutional Review Board approved the study protocol. All participants provided written informed consent. We collected the data for this study between August 2007 and November 2010. Community-dwelling spousal AD caregivers and non-caregiving married controls, matched in terms of age (≥55 years) and gender, were recruited into the UCSD "Alzheimer's Caregiver Study" investigating health consequences of dementia caregiving stress. Referrals were from the UCSD Alzheimer's Disease Research Center, community support groups, agencies serving caregivers, local senior citizen health fairs, and other participants. Exclusion criteria for caregivers and controls were current major illnesses (e.g., cancer), BP>200/120 mmHg, and certain medications (i.e., oral anticoagulants, non-selective beta blockers, and steroids).

We assessed participants in their homes every 12 months for a period of up to 3 years (i.e., for a maximum of 4 visits) and also asked them to call research staff whenever there was a transition in their caregiving situation or health status. Research staff also made brief follow-up phone calls every 3 months to check for caregiver transitions and changes in health status. If the caregiver had placed the AD spouse in a long-term care facility or a spouse had died, staff set up an appointment for the post-transition assessments that included collection of blood samples, which occurred at 3, 15, and 27 months after the transition.

At each assessment a research nurse gathered information on demographic factors, health behaviors, health status, and psychological distress using questionnaires; prescribed medications were also noted. For the biochemical assessment of measures for the estimation of GFR (including creatinine), participants had their blood collected between 10:00 and 10:45 AM. Fasting state was not a requirement in order to not interfere with caregivers' daily routine. The study reports on 119 caregivers and 58 non-caregivers with complete baseline data out of the total enrolment of 186 study participants (126 caregivers, 60 non-caregiving controls).

Measures

Sociodemographic factors—We collected information on gender, age, ethnicity, years of education (reflecting socioeconomic status), and years of caregiving.

Medical history and current medication—Participants were asked to indicate whether a doctor had informed them that they currently have or ever had "hypertension", "diabetes", kidney problems" and various "cardiovascular diseases" (i.e., myocardial infarction, congestive heart failure, angina, other heart diseases, stroke/transient ischemic attack) which were aggregated into one category. BP- lowering drugs (e.g., diuretics) and cholesterol-lowering drugs (e.g., statins) were aggregated into one medication category each.

Acute health symptoms—To account for a potential impact of acute medical events on the shorter-term worsening of GFR (e.g. through fever or dehydration), participants were asked whether they had experienced any one (yes/no) of the following symptoms in the last month: temperature ≥38o C, nausea or vomiting, diarrhea, bloody stools, shortness of breath, chest pain, pounding heart, unplanned weight loss.

Body mass index—We calculated BMI based on subjects' self report of weight and height by dividing weight in kilograms by the square of height in meters.

Blood pressure—The research nurse collected three seated BP measurements after a 15-minute resting period using a non-invasive Microlife Blood Pressure monitor. The average was computed and taken as the participant's mean systolic and diastolic baseline BP.

Health behaviors—Smoking status was defined as never smoked vs. ever smoked (i.e., former or current smoking; only two participants were current smokers at the baseline assessment). Alcohol consumption during the last month was assessed by multiplying the number of days subjects had at least one alcoholic drink by the number of alcoholic drinks they usually drank on those days (total score 0–36). The Rapid Assessment of Physical Activity (RAPA) scale was used to assess caregivers' amount of physical activities of varying intensity (i.e., light, moderate, vigorous) in a typical week, including strength and flexibility exercises (total score 0–6) (31).

Psychological distress—The short form of the Center for Epidemiologic Studies-Depression scale (CESD-10) was used to assess the level of depressed mood (32). Role overload with life responsibilities was rated using a 4 item scale (33); for example "you work hard (as a caregiver) but never seem to make any progress." Average responses to each item (1 = not at all, 4 = completely) were used to create a total overload score (range 1–4).

Laboratory measurements—Plasma creatinine, blood urea nitrogen, serum albumin, and hemoglobin were determined by standard methodology at the clinical chemistry laboratories at the UCSD Medical Center. The same creatinine assay method was kept during the study (Roche Diagnostics Cobas 6000 c501 Module Clinical Chemistry Analyzer).

Kidney function—The GFR was estimated using a previously published Modification of Diet in Renal Disease (MDRD) Study formula (34):

$$eGFR\,(mL/min/1.73m^2) = 170 * serum\ creatinine^{-0.999} * age^{-0.176} * blood\ urea\ nitrogen^{-0.170} * albumin^{+0.318} * [0.762\ if\ female] * [1.180\ if\ African\ American]$$

. A GFR of less than 60 mL/min per 1.73 m^2 reflects loss of at least half of the normal level of kidney function (21).

Data Analysis

Data were analyzed with PASW 18.0 statistical software package (SPSS Inc., Chicago, IL). Level of significance was set at p≤0.05 (2-tailed). Mann-Whitney and chi-square tests were used to compare caregivers and non-caregivers on baseline characteristics. Before analysis, normal distribution of GFR was assured by the Kolmogorov-Smirnov test.

We conducted a mixed (random-effects) regression analysis to examine the impact of caregiver transitions (i.e., placement and death of the spouse) on GFR (35). To increase the interpretability of regression coefficients and to diminish problems associated with multicollinearity, we centered independent variables before conducting analysis (36)except "time" (in years) which was linear in nature with the baseline assessment coded as "0." Linear variables were centered around their grand means and dummy coded categorical variables were centered at −0.5 (e.g., non-caregivers) and + 0.5 (e.g., caregivers). The model included the following fixed effects: caregiving status, education, history of several diseases (i.e., hypertension, diabetes, CVD, and kidney problems), hemoglobin, medication categories (BP- and cholesterol-lowering drugs), acute health symptoms, smoking status, BMI, physical activity, alcohol consumption, depressive symptoms, role overload, placement status of the AD spouse (0=no placement, 1=placed), and deceased status of the spouse (0=not deceased, 1=deceased). Of these, history of diseases, hemoglobin, medication categories, acute health symptoms, smoking status, BMI, physical activity, alcohol consumption, depressive symptoms, role overload and placement and deceased status of the spouse were all entered as time-varying. We made no adjustments for gender, age, and ethnicity as all of these variables are already considered for the calculation of the GFR with the MDRD formula (34). Random intercepts were modelled for participants. A significant effect of placement and/or spousal death would mean that there was a change in the GFR intercept as a function of the transition (i.e., from pre- to post-transition). In other words, the coefficient for transitions is interpreted as a change in the intercept upon transitions. The value of the coefficient applies to all post-transition visits meaning that a drop in the GFR of a certain magnitude at 3 months after a transition is interpreted to maintain across all post-transition visits (note that all post-transition visits were coded as “1” and all pre-transition visits were coded as “0”).

Because the effect of transitions on GFR was assumed to be moderated by psychological distress and CKD risk factors, we probed for interactions between transitions and depressed mood, role overload, and those CKD risk factors that turned out to be significant independent predictors of GFR in our model. In case of a significant interaction, we applied the Holmbeck method (37) to test whether high levels (+1 standard deviation from the mean) vs. low levels (−1 standard deviation from the mean) of a continuously scaled moderator variable would alter the relation between caregiving transitions and GFR.

For the 177 participants, there were a total of 500 assessments. This number of observations allowed us to adjust for a number of 19 prespecified covariates (detailed above) in the mixed regression analysis without overfitting our model (38). However, to guard against a residual possibility of over-modeling, we additionally computed a simplified model with only caregiver status, time, placement of the AD spouse and spousal death as covariates.

Time-variant variables were complete in 100% of cases for medication and physical activity; in 98.6% for history of hypertension, CVD and kidney problems, and for alcohol consumption, acute health symptoms, depressive symptoms, and role overload; in 98.4% for diabetes history, smoking status, and BMI; in 94.2% for GFR; in 93.4% for BP; and in 92.8% for hemoglobin.

RESULTS

Baseline Characteristics of Study Participants

The mean age±SD of all participants was 74.5±7.5 years (range 54.7–90.4) and 68.9% were women. The sample comprised 92.1% Caucasians, 2.8% African Americans, and 5.1% other ethnicities. Mean GFR was 79.1±19.0 mL/min/1.73m^2 (range 8.3–151.2) with 13.6% of participants having a GFR <60 mL/min/1.73m^2. Caregivers had been providing care to their AD spouse for an average of 4.4±3.4 years (range 0.5–17.1). Compared to their non-caregiving counterparts, caregivers had expectedly higher levels of depressed mood and role overload. Caregivers also were significantly less physically active and reported more frequently any acute health symptom in the last month relative to non-caregivers (Table 1). There were no significant differences in other health behaviors, sociodemographic factors, medical data (including the GFR) between caregivers and non-caregiving controls at baseline.

Transitions

Over the course of the study, 30 (25.2%) caregivers placed their spouses in a long-term care facility and 19 (16.0%) experienced the death of their spouses (in 6 cases the AD spouse had died after placement in a long-term care facility). Five (8.6%) spouses of the non-caregivers also died. The initial post-transition assessments occurred at 3 months following placement or death of the spouse. The remaining assessments took place approximately 12 months (12 placements, 8 caregiver spouses deceased, 1 non-caregiver spouse deceased) or 24 months (2 placements) later.

Predictors of the Estimated Glomerular Filtration Rate

The linear mixed regression model for the GFR over the study period is given in Table 2. The GFR showed a significant increase with each assessment the participants were in the study (i.e., main effect of time) (p=.03). There was no significant difference between caregivers and non-caregivers in mean GFR over time (i.e., main effect for caregiver status) (p=.77). The estimated annual GFR values (mL/min/1.73m^2)for caregivers were 69.43±4.11 (n=119), 60.64±6.47 (n=114), and 72.45±5.19 (n=86), for baseline, year 1, and 2, respectively. For controls, these values were 69.11±5.06 (n=58), 62.07±7.39 (n=58), and 73.49±7.03 (n=43). The model for year 3 data could not be fitted because the number of observations from the 15 caregivers and 7 controls with year 3 data was less than the number of model parameters.

Testing our secondary hypothesis about effects of transitions revealed that when spouses of caregivers were placed in a long-term care facility a significant decline in caregivers' GFR was observed in the subsequent 3-month follow-up assessment (change GFR = −4.93±2.22 mL/min/1.73m2 (p=.03). A similar effect of death of the spouse on GFR was found, but the change did not reach statistical significance (4.37±2.55 mL/min/1.73m2, p=.09). This results remained the same when the 5 non-caregivers whose spouse had deceased were excluded from the analysis (4.43±2.69 mL/min/1.73m2, p=.10).

These relationships were essentially maintained in a complementary model which considered caregiver status, time, placement of the AD spouse and spousal death as the sole covariates. In this model placement of the AD spouse and spousal death were related to a decrease in the GFR of 6.21±2.02 mL/min/1.73m^2 (p=.002) and 2.77±2.43 mL/min/1.73m^2 (p=.26), respectively. Caregiving was associated with a non-significant increase in the GFR over time of 0.90±2.89 mL/min/1.73m^2 (p=.76). The estimated annual GFR values (mL/min/1.73m^2)for caregivers were 79.63±1.74, 74.26±4.30, 76.37±2.70, and 77.60±12.29 for baseline, year 1, 2, and 3, respectively. For controls, these values were 77.92±2.50, 73.97±5.19, 76.09±4.59, and 74.74±15.05. Also, no significant association emerged between spousal death and change in the GFR when the 5 non-caregivers whose spouse had deceased were excluded from this complementary analysis (p=.27).

As can also be seen in Table 2, a positive history of hypertension (p=.045) and of diabetes (p=.02), lower hemoglobin values (p=.03) and lower amount of regular alcohol consumption (p=.03) were all significantly predictive of a reduction in GFR over time.

Moderating Variables of Caregiving and Transition Effects on GFR

Caregiving status—There were no significant interactions between caregiving status and depressive symptoms (p=.45), role overload (p=.41), hypertension history (p=.16), diabetes history (p=.33), hemoglobin (p=.50), and alcohol consumption (p=.13) for changes over time in the GFR.

Placement of the AD spouse—There was a significant interaction between placement and hypertension history for GFR (−8.03±3.83, p=.04). In caregivers with a positive history of hypertension, placement was associated with a decline in the GFR by 5.65±3.12 mL/min/ $1.73m^2$ (p=.07), whereas there was a decrease of only 2.35±3.36 mL/min/$1.73m^2$ (p=.49) in participants without a history of hypertension. When hypertension status was replaced by continuous BP measurements, there emerged a significant interaction between placement and diastolic BP (−0.37±0.18, p=.047) but not between placement and systolic BP (p=.33) in predicting GFR. Post hoc probing of this significant interaction suggested that placement resulted in a decrease in GFR particularly in caregivers with high diastolic BP levels at 3 months post-placement. More specifically, there was a significant decline in GFR by 8.33±2.88 mL/min/$1.73m^2$ if diastolic BP was high (p=.004), but not if diastolic BP was low (−1.43±2.70 mL/min/$1.73m^2$, p=.60) at 3 months post-placement. No three-way interaction emerged between placement, hypertension history and diastolic BP (p=.68); this suggests that the decline in GFR in caregivers with high diastolic BP levels at post-placement was unrelated to hypertension history. Placement did not significantly interact with depressive symptoms (p=.75), role overload (p=.34), diabetes history (p=.15), hemoglobin (p=.82), and alcohol consumption (p=.93) in predicting a change in the GFR.

Death of the spouse—There was a significant interaction between spousal death and hypertension history for GFR (9.06±4.40, p=.04) which, however, became non-significant if the 5 non-caregivers whose spouse had deceased were excluded from the analysis (p=.08). Replacing hypertension status by continuous BP measurements revealed non-significant interactions between spousal death and both systolic BP (p=.78) and diastolic BP (p=.46) for a change in the GFR. The same was found when excluding the 5 non-caregivers whose spouse had died from the analysis (p-values >.62).

Spousal death did not significantly interact with depressive symptoms (p=.91), role overload (p=.41), diabetes history (p=.15), hemoglobin (p=.94), and alcohol consumption (p=.26), respectively, in predicting a change in the GFR. Spousal death also did not significantly interact with these variables, when the five non-caregivers whose spouses had deceased were not considered for the analysis (all p-values >.16).

DISCUSSION

We studied the GFR in chronically stressed AD caregivers who are a group at increased risk of CVD (2–8). As CVD and CKD share so many major risk factors (20, 21, 25), AD caregivers might also be prone to CKD. Consistent with the literature (3, 39), caregivers perceived significantly more distress in the form of depressive symptoms and role overload and they reported also more physical health symptoms and lower level of physical activity than their non-caregiving counterparts at baseline; no significant group differences emerged in other health characteristics at baseline. Approximately 14% of our study participants and 17% of persons older than 60 years in the US population (40) show an estimated GFR less than 60 mL/min/$1.73m^2$. Regarding the proportion of subjects with low kidney function, our sample is thus comparable with the elderly general US population.

One major finding from our study is that GFR did not significantly differ between caregivers and non-caregivers over the entire study period of up to three years. This relationship was also not significantly moderated by the level of psychological distress and risk factors of CKD, including hypertension. However, observation periods beyond three years might be needed to detect significant effects of psychosocial factors on kidney function (16–19). The development of borderline hypertension in AD caregivers compared to non-caregiving may well take three years as well (29). Therefore, our average study observation period during which caregiving burden might impact kidney function was possibly too short to yield detectable group differences. Moreover, limited statistical power might be another explanation for these non-significant findings (e.g., only 15 caregivers and 7 controls contributed year 3 data).

We further found that caregivers who placed their AD spouse in a nursing home experienced a significant drop in GFR at 3 months after placement. This finding concurs with the notion that transition of the care recipient out of home does not uniformly relieve caregiver distress or improve caregiver health (41, 42). While some burdens are lessened when a spouse is placed, others persist, or may even increase. For example, the caregiver may have added worries as to the treatment the spouse is receiving in the care facility, may visit regularly and provide help, or may worry about costs (28). In agreement with previous research (24, 25, 43), a positive history of hypertension and of diabetes, as well as lower levels of hemoglobin and of alcohol consumption all significantly predicted reduction in GFR over time. Of these, hypertension status significantly interacted with placement status to predict GFR. Caregivers with a positive history of hypertension showed a greater decline in GFR at 3 months post-placement relative to participants without a hypertension history. Similar results emerged when we replaced hypertension history with diastolic BP values to identify more subtle effects of placement associated BP changes on GFR.

Research shows greater sympathoadrenal medullary arousal in AD caregivers than in non-caregiving controls (44) and placement of the AD spouse was associated with an increased BP reactivity in caregivers (30). Moreover, there was an inverse association between GFR and BP responses to acute mental stress in subjects >55 years (45). It is also well known that BP increase may hamper glomerular function (25). As a whole, the findings from these studies suggest that those caregivers showing a drop in GFR post-placement in association with higher BP might have experienced exaggerated sympathetic activation when the AD spouse transitioned to a long-term care facility.

In those caregivers with a positive history of hypertension and with 1 SD above the mean values for diastolic BP, respectively, we found a covariate-adjusted decline in GFR of 6 and 8 mL/min/1.73m^2 at three months after placement of the AD spouse. Complications of CKD usually start to appear below a GFR of 60 mL/min/1.73m^2 (21) and only 15.1% of our caregivers had a GFR this low. The size of the effect of placement on GFR in those with high BP (i.e., ≈10 mL/min/1.73m^2) may all the same be clinically relevant in terms of caregivers' CVD risk, even in those caregivers with a GFR greater than 60 mL/min/1.73m^2. This is illustrated by data from the Cardiovascular Health Study in which individuals 65 years of age or older and with GFR values (range 15–130 mL/min/1.73 m^2)comparable to those of our subjects (range 8–151 mL/min/1.73 m^2), showed an adjusted hazard ratio for de novo CVD of 1.07 (95% CI 1.01–1.12) for each 10 mL/min/1.73 m^2 decrease in GFR (46).

In contrast to placement, we did not observe that GFR was significantly affected by the death of the spouse (p=.09), even when we excluded from the analysis non-caregivers whose spouses had deceased from the analysis (p=.10). However, the size of these p-values suggests the effect of spousal death on kidney function might have been significant with a larger sample size. In fact the estimated average effects of placement and death of the AD spouse on GFR were barely different in absolute terms (−4.9 vs. −4.4), so the difference in statistical significance for placement and not spousal death seems primarily a matter of arbitrary statistical cut points.

Our study has several limitations. The findings might not generalize to younger populations, the elderly with poor physical health and particularly those with more impaired kidney function and more severe hypertension. Although widely used in clinical studies, the MDRD formula to compute the GFR provides only an estimate of the "true" kidney function. We obtained a history on "kidney problems" but we did not specifically ask participants about kidney diseases with a clearly increased risk for CKD, including glomerulonephritis and polycystic kidney disease. Medical history was by self-report which may introduce unreliability into disease and medication categories, although previous studies showed good agreement between medical charts and self-report of diseases and drug intake (47, 48). The self-report of height (but less so of weight) in individuals 70 years and older may be problematic in that BMI was shown to be one unit lower when computed with self-reported height than when calculated from measured height (49). We controlled for a number of factors potentially impairing renal function, including acute medical symptoms in the month prior to the assessment of GFR. While this approach may be jeopardized by over-modeling, results from a simplified model implied our multivariate analysis was reliable. However, there might be additional confounding factors we did not systematically assess in our study. For instance, hospitalization of the caregiver due to acute medical events might result in definite placement of the care recipient and also in transient changes of the dosage of antihypertensive drugs and prescription of new medications (e.g. antibiotics and non-steroidal anti-inflammatory drugs) all having the potential to impair GFR. We did not collect data on medication adherence; there is a possibility that the effect of elevated BP on GFR after placement reflects poor compliance with prescribed antihypertensive drugs. Whether the immediate decline in kidney function in caregivers will sustain beyond 3 months after a major transition in the caregiving situation remains unclear.

Taken together, the findings from this study show that placement of an AD spouse in a nursing home is associated with lessened kidney function in caregivers at 3 months after placement. The same effect might apply to the death of the AD spouse, although statistical power was limited to definitely prove this observation. Previous studies suggest AD caregivers are at increased risk to develop hypertension (29) and thus their kidney function might profit from close monitoring of BP. Our study adds to this notion and may suggest that the subgroup of caregivers with concomitantly increased BP post-placement might be particularly vulnerable to experience a decline in GFR. Therefore, clinicians could be encouraged to closely monitor BP in AD caregivers in general and particularly so in those who have recently placed their spouse in a long-term care facility. In this group of caregivers, elevated BP should probably be rigorously treated based on current guidelines.

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Acronyms Used in the Text

AD	Alzheimer's disease
BMI	body mass index
BP	blood pressure
CKD	chronic kidney disease
CVD	cardiovascular disease
GFR	glomerular filtration rate
MDRD	Modification of Diet in Renal Disease
SES	socioeconomic status

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Table 1

Baseline Characteristics of 177 Study Participants

Variables	**Caregivers (n=119)**	**Non-caregivers (n=58)**	***P*-value**
Gender (female) (%)	69.7	67.2	.74
Age (years)	74.4±8.1	74.9±6.2	.98
Caucasian (%)	95.0	86.2	.07
Education (years)	15.1±3.1	15.8±3.2	.07
History of hypertension (%)	56.3	43.1	.10
Systolic blood pressure (mmHg)	134.4±15.4	133.3±15.6	.50
Diastolic blood pressure (mmHg)	75.8±8.6	73.0±10.3	.07
History of diabetes (%)	12.6	3.4	.06
History of cardiovascular disease (%)	17.6	8.6	.17
History of kidney problems (%)	5.0	3.4	1.00
Blood pressure-lowering medication (%)	60.5	53.4	.37
Cholesterol-lowering medication (%)	47.1	44.8	.78
Acute health symptoms (%)	31.9	8.6	.001
Ever smoker (%)	46.2	38.6	.34
Body mass index (kg/m^2)	26.6±4.8	26.2±6.0	.25
Physical activity (score)	3.40±1.65	4.00±1.55	.01
Alcohol consumption (score)	5.51±4.79	5.67±6.09	.80
Depressive symptoms (score)	8.63±5.85	2.64±4.16	<.001
Role overload (score)	5.16±3.19	1.38±1.94	<.001
Glomerular filtration rate (mL/min/1.73m^2)	79.6±20.1	77.9±16.6	.40
Glomerular filtration rate <60 mL/min/1.73m^2 (%)	15.1	10.3	.49
Plasma creatinine (mg/dL)	0.87±0.45	0.86±0.21	.43
Blood urea nitrogen (mg/dL)	17.1±6.5	16.4±4.8	.96
Serum albumin (g/dL)	3.77±0.25	3.73±0.24	.37
Hemoglobin (g/dL)	13.0±1.3	13.0±1.2	.97

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Table 2

Predictors of Glomerular Filtration Rate (GFR) Over Time

Variables	Estimate	S.E.	P-value
Intercept	70.68	3.06	<.001
Caregiver status	0.89	3.02	.77
Education	−0.40	0.42	.35
History of hypertension	−3.49	1.73	.045
History of diabetes	−7.36	3.12	.02
History of cardiovascular disease	−1.76	2.18	.42
History of kidney problems	−1.12	3.34	.74
Hemoglobin	1.61	0.75	.03
Blood pressure−lowering medication	−1.78	1.82	.33
Cholesterol-lowering medication	−1.51	1.60	.35
Acute health symptoms	2.22	1.46	.13
Ever smoker	−3.87	2.08	.06
Body mass index	−0.03	0.20	.87
Physical activity	−0.21	0.41	.61
Alcohol consumption	0.33	0.15	.03
Depressive symptoms	0.17	0.15	.25
Role overload	−0.08	0.28	.78
Time	1.27	0.60	.03
Placed spouse	−4.93	2.22	.03
Spouse deceased	−4.37	2.55	.09

All variables were centered to the mean such that the intercept shows the average GFR in the entire sample. Categorical variables were contrast coded (+0.5 vs. −0.5) with +0.5 being assigned to caregivers, those with hypertension, diabetes, cardiovascular disease, and kidney disease, those taking antihypertensive drugs and cholesterol-lowering drugs, those with any acute health symptom, and to ever smokers. “Placed Spouse” and “Spouse Deceased” indicate the immediate change in the GFR assessed 3 months after the respective transition. “Time” indicates the change in the GFR per each assessment the participant was in the study.