Short-term change in kidney function and risk of end-stage renal disease

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Abstract

Background. It is unclear what degree of change in the eGFR over a 1-year period indicates clinically significant progression, and whether this change adds additional information beyond that obtained by a single eGFR measure alone.

Methods. We included 598 397 adults who had at least two outpatient eGFR measurements (at least 6 months apart) during 1-year accrual period in Alberta, Canada. Change in kidney function (using the first and last eGFR) was defined by change in kidney function category with confirmation based on percent (%) change in eGFR [(last eGFR – first eGFR)/first eGFR × 100]. The groups for change in kidney function were thus defined as: ‘certain drop’ (drop in CKD category with ≥25% decrease in the eGFR); ‘uncertain drop’ (drop in CKD category with <25% decrease in the eGFR); ‘stable’ (no change in CKD category); ‘uncertain rise’ (rise in CKD category with <25% rise in the eGFR) and ‘certain rise’ (rise in CKD category with ≥25% increase in the eGFR). Adjusted end-stage renal disease (ESRD) rates (per 1000 person-years) for each group of change in kidney function were calculated using Poisson regression. Adjusted risks of ESRD associated with change in kidney function, in reference to stable kidney function, were estimated.

Results. Among the 598 397 participants, 74.8% (n = 447 570) had stable (no change in CKD category), 3.3% (n = 19 591) had a certain drop and 3.7% (n = 22 171) had a certain rise in kidney function. Participants who experienced a certain change in kidney function (both drop and rise) were older, more likely to be female, and had a higher prevalence of comorbidities, in comparison with those with stable kidney function. There were 1966 (0.3%) ESRD events over a median follow-up of 3.5 years. Compared with participants with stable kidney function, after adjustment for covariates, and the first eGFR measurement, those with certain drop had 5-fold increased risk of ESRD (HR: 5.11; 95% CI: 4.56–5.71), whereas those with an uncertain drop had 2-fold increased risk (HR: 2.13; 95% CI: 1.84–2.47). After adjustment for the eGFR and covariates at the last visit, neither a certain nor uncertain drop in the eGFR was associated with an increased ESRD risk. The ESRD risk associated with the last eGFR level, adjusted for the slope over time, were 2.89 (95% CI: 2.35–3.55), 10.98 (95% CI: 8.69–13.87), 35.20 (95% CI: 27.95–44.32) and 147.96 (116.92–187.23) for categories 2, 3a, 3b and 4, respectively, in reference to category 1.

Conclusions. A change in eGFR category accompanied by ≥25% decline (certain drop) is associated with increased ESRD risk. However, this elevated risk is captured by patient characteristics and eGFR at the last visit, suggesting that eGFR trajectories based on more than two serum creatinine measurements over a period longer than 1 year are required to determine ESRD risk and allow more reliable risk prediction.

Keywords: change in eGFR; chronic kidney disease; CKD stages; end-stage renal disease; population

Introduction

An association between more severely impaired kidney function and future risk of end-stage renal disease (ESRD) has been reported [1–5]. These studies however have predominantly considered kidney function at one point in time and did not assess the association between change in kidney function and future risk. Understanding the dynamics of change in kidney function using serial kidney function measurements may contribute additional prognostic information beyond a single measurement. This could be further enhanced by incorporating the rate of decline of kidney function in the risk classification to identify patients who are at a
greater risk of ESRD. Although a limited number of studies have demonstrated an association between change in kidney function over time and adverse outcomes [6–10], these studies have focused on cardiovascular disease or all-cause mortality. The association between change in kidney function and risk of ESRD specifically has not been well studied.

Conventionally the rate of change in kidney function has been assessed in an annualized form based on pooled measures of the eGFR across multiple years—the prognostic value of which depends on the number of eGFR measures, the duration of follow-up and the linearity of progression. Each of these measures of the eGFR contains information on kidney function and systematic and random effects on creatinine—complicating the estimation and extrapolation of patient trajectories. In contrast, 1-year change in kidney function based on two measures of the eGFR is simpler to calculate and could have well-defined prognostic implications. Although an annual update of eGFR is arguably the most clinically used measure of progression, the association between changes in kidney function over 1-year and risk of ESRD has not been studied.

Using a large community-based cohort, we tested the hypothesis that a certain drop in kidney function (defined as a change in eGFR category confirmed by a 25% or greater drop in eGFR), over a 1-year time period was associated with an increased risk of ESRD, independent of baseline kidney function.

Methods

Study population and data sources

The Alberta Kidney Disease Network (AKDN) data repository [11] was used for this retrospective cohort study. The study population included adults (aged ≥18 years) in Alberta, Canada who had at least two outpatient creatinine measurements (at least 6 months apart) within a 1-year period (Figure 1). Cohort accrual occurred from 1 May 2002 to 31 March 2008, with follow-up to 31 March 2009 (to ensure at least 1 year of follow-up). Patients were excluded if they were treated with dialysis or a kidney transplant at baseline. Among 1 818 451 patients with at least one outpatient serum creatinine measurement, we identified 865 851 participants aged 18 years and older with two or more measurements in a 1-year period. We further excluded 156 participants with the baseline eGFR <15 mL/min/1.73 m², 1045 with 24 or more measurements in a 1-year period (possibly indicating unstable kidney function or frequent illness) and 266 253 with measurements separated by ≤6 months, for a final cohort of 598 397 (Figure 2).

Change in kidney function

The first and last creatinine measurement during the 1-year accrual period was used to estimate GFR using the CKD-EPI equation [12]. Although data on race were not available from the data sources, <1% of the Alberta population is black [13]. The eGFR was divided into the following categories: 1, 2, 3a, 3b, 4 and 5 (≥90, 60–89.9, 45–59.9, 30–44.9, 15–29.9 and <15 mL/min/1.73 m², respectively). Change in kidney function (using the first and last eGFR) was defined by the change in eGFR category with confirmation based on percent (%) change in eGFR [(last eGFR – first eGFR)/first eGFR × 100]. The groups for change in kidney function were thus defined as: ‘certain drop’ (drop in CKD category with ≥25% decrease in eGFR); ‘stable’ (no change in CKD category); ‘uncertain drop’ (rise in CKD category with <25% decrease in eGFR); ‘certain rise’ (rise in CKD category with ≥25% increase in eGFR). Similar to other studies [9, 14], a 25% change in the eGFR was used to define certainty of change as this degree would reflect a true change in kidney function rather than variability in creatinine measurements related to the assay [15] or intra-individual serum creatinine variation across measurements [16].

Participants’ sociodemographic characteristics were determined from the administrative data files of the provincial health ministry (Alberta Health and Wellness). First Nation status was determined using the registry file. Although it was not possible to identify other race/ethnic groups, over 85% of the Alberta population is Caucasian [13]. Socioeconomic status was categorized as high income (annual adjusted taxable family income ≥$39 250 CAD), low income (annual adjusted taxable family income <$39 250 CAD), low income with subsidy (receiving social assistance) and pensioners (65 years of age and older) based on

Fig. 1. Overview of cohort creation and study period.
of diabetes mellitus and hypertension were identified from hospital discharge records and physician claims based on validated algorithms [18, 19]. Other comorbid conditions based on the Deyo classification of Charlson comorbidities were identified from the physician claims and hospitalization records using validated ICD-9-CM and ICD-10 coding algorithms [20]. Proteinuria was estimated by urine albumin:creatinine ratio (ACR) or urine dipstick based on outpatient random spot urine measurements in the 6 months before and after the index eGFR measurement. Proteinuria was categorized as normal, mild, heavy or unmeasured based on ACR [normal (ACR <30 mg/g), mild (ACR 30–300 mg/g) or heavy (ACR >300 mg/g)] or urine dipstick [(urine dipstick negative); mild (urine dipstick trace or 1+) or heavy (urine dipstick 2+)], as previously described [1, 21].

Outcome ascertainment

Outcome ascertainment started from the date of the last creatinine measurement in the 1-year accrual period to end of study (31 March 2009). The outcome was the development of ESRD, defined as the date of registration for chronic dialysis or renal transplantation determined from the renal program databases [22].

Statistical analyses

Adjusted ESRD rates (per 1000 person-years) for each group of change in kidney function were calculated using Poisson regression by substituting the means or frequencies, as appropriate, for the sociodemographic variables, kidney function, proteinuria and covariates as shown in Table 1. Adjusted rates were estimated separately for the first and last eGFR measurement by adjusting for covariates at the corresponding time point. If the Poisson assumption, that the outcome variance equals its mean was not met, a quasi-Poisson model was used [23]. Cox proportional hazards models were used to estimate the adjusted risk of ESRD. The association between percent change in the eGFR and ESRD, separately with adjustments at the time points of the first and last eGFR measurement. We used a restricted cubic spline function with five knots to plot this relationship, which allows for the assessment of non-linear effects of the exposure-outcome relationship.

We did several sensitivity analyses to confirm our study findings. We repeated analyses using alternate definitions for the time span to define change in kidney function, considering a span of <6 months, 6–9 months and 9–12 months, in addition to the 6 to 12 months used in our primary analysis. We also defined the category change based on 15 or 35% drop in eGFR values. We also repeated all analyses stratified by CKD category, both at first and last measurement. Statistical analyses were performed using the SAS version 9.2 (SAS Institute, Inc., Cary, NC, USA), STATA version 10.1 (STATA Corp, College Station, TX, USA) and R program (version 2.13.1). The institutional review board of the University of Calgary approved the study.

Results

Participant characteristics by change in kidney function groups are shown in Table 1. Of the 598 397 eligible participants, 74.8% (n = 447 570) had stable (no change in CKD category), 3.3% (n = 19 591) had a certain drop and 3.7% (n = 22 171) had a certain rise in kidney function. Participants who experienced a certain change in kidney function (both drop and rise) were older, more likely to be female, and had a higher prevalence of comorbidities, in comparison with those with stable kidney function.

There were 1966 (0.3%) ESRD events over a median follow-up of 3.5 years. The unadjusted rates of ESRD were highest for those with a certain drop in kidney function (rate 6.79 per 1000 person-years; 95% CI: 6.77–6.81) (Table 2). With multivariate adjustment at the first (baseline) eGFR measurement, the highest rate was observed for a certain drop in kidney function (rate 0.77 per 1000 person-years; 95% CI: 0.44–1.10); conversely with multivariate adjustment at the last eGFR measurement, the highest rate was observed for certain rise in kidney function (rate 0.36 per 1000 person-years; 95% CI: 0.16–0.55).

Compared with participants with stable kidney function, the unadjusted risk of ESRD was 10-fold higher (HR: 10.37; 95% CI: 9.34–11.50) for those with a certain drop in kidney function followed by uncertain drop in kidney function (HR: 1.49; 95% CI: 1.29–1.72) (Figure 3A). The risk for certain drop was 5-fold higher (HR: 5.11; 95% CI: 4.56–5.71) when adjusted for covariates at the first eGFR measurement (Figure 3B). In contrast, risk was no longer present when adjustments were performed for covariates at the last eGFR measurement (Figure 3C), suggesting that extrapolation of a 1-year decline in kidney function does not add information regarding the risk of ESRD beyond that of the last measurement of eGFR alone.

We further assessed the risk of ESRD associated with the last eGFR measurement specifically, divided into categories 1, 2, 3a, 3b and 4 and adjusting for covariates and 1-year change in kidney function. Relative to category 1, the adjusted risk of ESRD associated with category 2, 3a, 3b and 4 was 2.89 (95% CI: 2.35–3.55), 10.98 (95% CI: 8.69–13.87), 35.20 (95% CI: 27.95–44.32) and 147.96 (116.92–187.23), respectively, demonstrating the increased risk of ESRD with lower categories of kidney function based on the last eGFR measurement.

The relationship between percent change in the eGFR as a continuous variable and risk of ESRD is shown in...
Figure 4. The unadjusted and adjusted (for covariates at the first measurement) risk of ESRD increased in a near exponential fashion with decline in kidney function defined by percent decrease in the eGFR. This association disappeared when adjustment for covariates were done at the last measurement of the eGFR.

Sensitivity analysis

Similar results were observed in analyses considering different time spans for the assessment of kidney function (that is considering a span of <6 months, 6–9 months and 9–12 months between the first and last eGFR measurements) or redefining the category change based on 15% or 35% change in the eGFR (data not shown). We also found a similar association between change in kidney function and ESRD risk in analyses stratified by the baseline eGFR (Appendix Tables 1 and 2).

Discussion

In this large community-based cohort, we explored the association between change in kidney function over a 1-year period and risk of ESRD. We found that a certain drop in the eGFR (change in CKD category accompanied by a 25% decline from the baseline eGFR) was associated with an increased risk of ESRD—a risk that was independent of baseline kidney function, proteinuria and other covariates. However, when ESRD risk was assessed taking into account the last eGFR measurement, the 1-year change in kidney function was no longer associated with ESRD risk. This suggests that it is uninformative to extrapolate a rate of change based on two measures of eGFR alone over a 1-year period.

Though prior studies have reported an association between change in kidney function and risk of cardiovascular events or death [6–10], to the best of our knowledge this is the first population-based study to demonstrate the
association between short-term longitudinal changes in kidney function and risk of ESRD. Lee et al. [24], studying incident ESRD patients and rapid decline in kidney function, reported that 10% of ESRD cases are preceded by rapid decline in the eGFR. They defined rapid decline in kidney function if a patient was documented to have the eGFR >30 mL/min/1.73 m² within 3 months prior to the initiation of chronic dialysis. Although the eGFR has been described as decreasing linearly over time reflecting the structural renal function decline [25], a steeper decline over a short interval should alert the practitioner to the potential increased risk of ESRD and permit interventions to prevent or delay this potential increased risk. Initiating multidisciplinary care was reported to have significantly decreased the rate of fall of the eGFR [26, 27], the impact being the greatest in those patients whose eGFR was declining the fastest [26].

In the African American Study of Kidney Disease and Hypertension (AASK) [28, 29] clinical trial, ESRD risk was higher among participants with a lower decline in the eGFR (~1.19 mL/min/year/1.73 m², observed for the patients treated with amlodipine) in comparison with the patients with a relatively higher eGFR decline (~1.64 mL/min/year/1.73 m², observed for the patients treated with ramipril). The generalizability of these results, however, is limited due to the selective nature of the trial participants. We also observed a higher risk of ESRD with a certain rise in kidney function in the unadjusted analysis and analysis adjusted for covariates at the last measurement. Though our analysis included only outpatient serum creatinine measurements and further excluded those with multiple measurements which may be associated with episodes of acute kidney injury (AKI), the increased ESRD risk with rising kidney function may be attributable, in some extent, to resolving AKI. The statistical phenomenon of regression to the mean further suggests that the very low risk associated with the higher eGFR after a certain rise may overstate the case since some of the participants are likely to regress back toward their previous estimate of lower eGFR.

We found that the association between 1-year decline in kidney function and ESRD risk was no longer present after adjustment for kidney function and covariates at the last measurement. Further, the lower levels of kidney function itself at the last visit showed a graded increase ESRD risk independent of the previous change. These results suggest that a simple cross-sectional approach using the patient status at the last visit may be adequate in assessing risk of ESRD. This may be due to the fact that retrospective appraisal of change in the eGFR on ESRD risk (unlike prospective appraisal) is already captured in the patient’s achieved level of kidney function. Thus ESRD risk assessment could be performed based on the kidney function at the time of the patient visit. Although the risk of ESRD from a certain change in the eGFR disappears after adjustment for the last eGFR, if somebody is faced with a change in the eGFR and a risk assessment is needed, the consideration of prospective appraisal can help with that. Our results also suggest that more eGFR values over longer follow-up are required to decrease the signal-to-noise ratio and allow more reliable risk prediction. We could not conduct rigorous analysis of the sources and magnitude of variation in the eGFR in CKD patients. Though results of such an analysis would be unlikely to affect the conclusions of the current study, they would be useful to clinicians managing CKD patients, and to investigators designing progression trials.

Our study has a number of strengths including the ability to study a large community-dwelling population across a range of kidney function. We were also able to assess the effect of a 1-year change in eGFR adjusted for both baseline and last estimates of kidney function to assess the independent effect of change in kidney function in a specific common clinical situation. Our definition of a certain drop had the advantage of being relatively simple to calculate as well as resulting in a relatively constant adjusted relative hazard of ESRD across different baseline eGFR categories.

Our study also has limitations due to its observational nature. First, the cohort was limited to individuals who had outpatient serum creatinine measurements as part of routine care, and therefore does not include individuals who did not access medical services. Further, information on the indication for serum creatinine measurement is not available,
thus the cohort may have resulted in inclusion of patients with comorbid conditions, although we were able to adjust for comorbidity in our analyses. However, since we were interested in outcomes among subjects with an estimate of kidney function, this limitation does not invalidate our results. Finally, although we adjusted for demographic factors, measured comorbidities, kidney function and proteinuria, we were unable to adjust for body mass index, blood pressure control, cause of kidney disease and smoking status—variables that may be associated with

Fig. 3. (A) Unadjusted risk of ESRD by 1-year change in kidney function. (B) Risk of ESRD by 1-year change in kidney function adjusted for covariates at the first measurement. Models were adjusted for age, sex, diabetes, hypertension, socioeconomic status, kidney function, proteinuria and history of comorbidities at the first measurement. (C) Risk of ESRD by 1-year change in kidney function adjusted for covariates at the last measurement. Models were adjusted for age, sex, diabetes, hypertension, socioeconomic status, kidney function, proteinuria and history of comorbidities at the last measurement.

Fig. 4. (A) Spline plot of the unadjusted risk of ESRD as a function of 1-year percent change in eGFR with superimposed histogram of percentage of the population. The solid black line represents the point estimates of the adjusted HR of ESRD; the shaded area represents the 95% confidence bands. (B) Spline plot of the risk of ESRD as a function of 1-year percent change in eGFR adjusted for covariates at the first measurement with superimposed histogram of percentage of the population. The solid black line represents the point estimates of the adjusted HR of ESRD; the shaded area represents the 95% confidence bands. Models were adjusted for age, sex, diabetes, hypertension, socioeconomic status, kidney function, proteinuria and history of comorbidities at the first measurement. (C) Spline plot of the risk of ESRD as a function of 1-year percent change in eGFR adjusted for covariates at the last measurement with superimposed histogram of percentage of the population. The solid black line represents the point estimates of the adjusted HR of ESRD; the shaded area represents the 95% confidence bands. Models were adjusted for age, sex, diabetes, hypertension, socioeconomic status, kidney function, proteinuria and history of comorbidities at the last measurement.
change in kidney function—thus we cannot exclude the possibility of residual confounding. However, given the magnitude of the observed associations, residual confounding and further adjustment for these covariates are unlikely to alter our findings. Future studies should examine the effect of change, and specifically our proposed definition of a certain drop, in kidney function on other CKD outcomes.

In conclusion, these data provide an interpretation of change in kidney function based on two eGFR measures ~1 year apart with respect to ESRD risk. A drop in eGFR category confirmed by a drop from baseline of 25% or more (certain drop) is associated with a markedly higher risk of ESRD. However, if the elevated risk of ESRD is updated with the last eGFR, the previous 1-year change in eGFR does not add information, suggesting extrapolation of eGFR trajectories, in relation to future ESRD, might require data beyond a 1-year interval and incorporating more than two measures.

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Conflict of interest statement. None declared. Results presented in this paper have not been published previously in whole or part, except in abstract format.

Appendix

A1. Risk of ESRD, by baseline eGFR category and 1-year change in kidney function adjusted for covariates at the first measurement

<table>
<thead>
<tr>
<th>Change in kidney function</th>
<th>Certain drop</th>
<th>Uncertain drop</th>
<th>Stable</th>
<th>Uncertain rise</th>
<th>Certain rise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 (eGFR ≥90)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>47</td>
<td>31</td>
<td>137</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Population, n</td>
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<td>42,989</td>
<td>210,520</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Hazard ratio (95% CI)</td>
<td>4.49 (3.12–6.47)</td>
<td>1.08 (0.72–1.61)</td>
<td>Reference</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Stage 2 (eGFR 60–89.9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>97</td>
<td>38</td>
<td>190</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Population, n</td>
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<td>14,954</td>
<td>204,702</td>
<td>32,161</td>
<td>9935</td>
</tr>
<tr>
<td>Hazard ratio (95% CI)</td>
<td>5.20 (3.94–6.86)</td>
<td>1.96 (1.38–2.80)</td>
<td>Reference</td>
<td>0.38 (0.21–0.68)</td>
<td>0.63 (0.32–1.25)</td>
</tr>
<tr>
<td>Stage 3a (eGFR 45–59.9)</td>
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<td></td>
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<td>98</td>
<td>47</td>
<td>96</td>
<td>19</td>
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</tr>
<tr>
<td>Population, n</td>
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<td>48,58</td>
<td>26,694</td>
<td>9583</td>
<td>7120</td>
</tr>
<tr>
<td>Hazard ratio (95% CI)</td>
<td>5.57 (4.11–7.55)</td>
<td>1.86 (1.31–2.66)</td>
<td>Reference</td>
<td>0.65 (0.39–1.06)</td>
<td>0.58 (0.34–0.98)</td>
</tr>
<tr>
<td>Stage 3b (eGFR 30–44.9)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events, n</td>
<td>137</td>
<td>65</td>
<td>179</td>
<td>17</td>
<td>22</td>
</tr>
<tr>
<td>Population, n</td>
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<td>1138</td>
<td>11,111</td>
<td>2739</td>
<td>3682</td>
</tr>
<tr>
<td>Hazard ratio (95% CI)</td>
<td>4.02 (3.18–5.08)</td>
<td>2.31 (1.73–3.10)</td>
<td>Reference</td>
<td>0.42 (0.26–0.70)</td>
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<td>Stage 4 (eGFR 15–29.9)</td>
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<tr>
<td>Events, n</td>
<td>155</td>
<td>55</td>
<td>459</td>
<td>14</td>
<td>25</td>
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<tr>
<td>Population, n</td>
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<td>128</td>
<td>3543</td>
<td>515</td>
<td>1434</td>
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<tr>
<td>Hazard ratio (95% CI)</td>
<td>4.85 (4.01–5.87)</td>
<td>2.93 (2.20–3.91)</td>
<td>Reference</td>
<td>0.25 (0.15–0.43)</td>
<td>0.18 (0.12–0.27)</td>
</tr>
</tbody>
</table>

CI, confidence interval.
Hazard ratios are adjusted for age, sex, diabetes, hypertension, socioeconomic status, kidney function, proteinuria, and history of cancer, cerebrovascular disease, congestive heart failure, chronic obstructive pulmonary disease, dementia, metastatic solid tumor, myocardial infarction, mild liver disease, moderate or severe liver disease, paralysis, peptic ulcer disease, peripheral vascular disease and rheumatic disease at the time of the first measurement. Stable kidney function is the reference group for the hazard ratios.
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The effect of revascularization of renal artery stenosis on renal perfusion in patients with atherosclerotic renovascular disease

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Abstract

Background. Only a small fraction of patients with atherosclerotic renovascular disease (ARVD) treated with revascularization have improved renal function after the procedure. It has been suggested that this may be due to effects of renal microvascular disease. Our aim was to measure the effect of renal artery stenosis (RAS) revascularization on renal perfusion in patients with renovascular disease.

Methods. Seventeen renovascular disease patients were treated by dilatation of unilateral (N = 8) or bilateral (N = 9) RAS (N = 23 kidneys), mainly because of uncontrolled or refractory hypertension. The patients were studied before and after (103 ± 29 days) the procedure. Renal perfusion was measured using quantitative positron emission tomography (PET) perfusion imaging.

Results. Although renal perfusion correlated inversely with the degree of RAS in patients with renovascular disease, it did not change after revascularization.

Conclusions. Our data support the notion of former clinical trials that angiographic severity of RAS does not determine the response to revascularization. Quantitative PET perfusion imaging is a promising tool to noninvasively measure renal perfusion for the assessment of physiological impact of RAS.

Keywords: atherosclerotic renovascular disease; imaging; renal artery stenosis; revascularization

Introduction

Atherosclerotic renovascular disease (ARVD) has become an increasingly recognized clinical condition, especially in older [1] and in otherwise atherosclerosis-prone populations, such as patients with hypertension, chronic kidney disease (CKD), coronary heart disease, congestive heart failure and peripheral vascular disease [2–5].

This increase in prevalence has led to a dramatically growing use of percutaneous transluminal renal angioplasty (PTRA) during the past 20 years [6]. However, the results in investigations of renal functional or cardiovascular outcomes after the revascularization procedures have been very variable [7–9]. Recently, it has been suggested that the poor outcomes after the PTRA could be attributable to the damage in the stenotic kidney parenchyma, especially the reduction of microvascular density [10, 11], changes mainly evident at the cortical level, which control almost 80% of the total renal blood flow (RBF).