Quantification of Single-Kidney Function and Volume in Living Kidney Donors Using Dynamic Contrast-Enhanced MRI

Eli Eikefjord¹,² Erling Andersen¹,³ Erland Hodneland⁴,⁵ Einar Svarstad²,⁶ Arvid Lundervold¹,⁷ Jarle Rørvik¹,²

Keywords: dynamic contrast-enhanced MRI, iohexol glomerular filtration rate (GFR), kidney parenchymal volume, living kidney donor, single-kidney function

OBJECTIVE. The objective of our study was to investigate whether dynamic contrast-enhanced MRI (DCE-MRI) can detect differences and potential adaption in single-kidney parenchymal volume, blood flow, glomerular filtration rate (GFR), and filtration fraction in the remaining kidney of healthy donors compared with nondonors. Further, we evaluated the agreement in donor GFRs measured using DCE-MRI versus serum clearance of iohexol.

SUBJECTS AND METHODS. Twenty living kidney donors and 20 healthy control subjects underwent DCE-MRI and iohexol GFR. Renal parenchymal volume was assessed from maximum-signal-intensity maps. Single-kidney MRI measurements of blood flow and GFR were derived from parenchymal signal intensity–time curves fitted to a two-compartment filtration model. The Student t test, Pearson correlation coefficient, mean differences, and limits of agreement were applied to analyze MRI measurements between groups and agreement with iohexol GFR.

RESULTS. MRI findings showed significantly higher blood flow (difference in mean values of donors vs control subjects, 54%; p = 0.001), GFR (78%, p < 0.0001), and renal parenchymal volume (65%, p < 0.0001) in the single kidney of donors compared with the single kidney of healthy control subjects. In the donors, a proportional increase in blood flow and GFR resulted in a comparable filtration fraction, as was observed in the control subjects. Significant correlations were found between MRI-derived GFR and parenchymal volume (p < 0.0016) as well as with iohexol GFR (p < 0.0001). The mean difference between MRI-derived GFR and iohexol GFR was 14.0 mL/min, and the limits of agreement between MRI-derived GFR and iohexol GFR were −24.1 and 52.1 mL/min.

CONCLUSION. DCE-MRI–derived values for single-kidney function and volume in kidney donors were significantly higher than those in control subjects and suggest a future potential benefit of DCE-MRI for diagnostic and prognostic structural and functional assessments in living kidney donors.
DCE-MRI to Quantify Kidney Function and Volume

be found to be feasible for earlier detection, prognosis, prediction, and monitoring of treatment effects of several renal diseases [15–22]. The use of DCE-MRI in the predonation evaluation could provide a baseline for a more comprehensive and individualized follow-up in the postdonation phase. In donors at higher risk of disease and complications (e.g., elderly donors or donors with hypertension or marginal GFR) and in donors with postnephrectomy complications, the use of DCE-MRI could provide early detection of abnormal morphologic and functional adaption. A recent study suggests postoperative stability in renal function by 1 month after donation and that poor adaption status from this time may be predictive of later development of chronic kidney disease (CKD) [23]. Hence, DCE-MRI from this time might represent a diagnostic and prognostic tool to assess individualized kidney function at regular intervals. In addition, donors usually have regular (yearly) follow-up by nephrologists, and long-term results are often reported every 5 and 10 years as part of national quality surveys.

Traditionally, radiologic methods are used solely in the preoperative evaluation of potential renal donors. Clinical workup includes renal scintigraphy to determine single-kidney function and CT or ultrasound to determine renal volumes and vascular anatomy [24]. The drawbacks of CT and renal scintigraphy include ionizing radiation and, in the case of scintigraphy, also low spatial resolution with poor morphologic visualization. Alternative unenhanced MRI techniques, such as arterial spin-labeling (ASL) [7] and DWI [2], have recently been applied to investigate renal function in living kidney donors. However, compared with DCE-MRI, those unenhanced techniques do not provide information about the GFR or filtration fraction.

GFR measurement using serum clearance of iohexol is an accepted alternative to the reference standard of the urinary inulin clearance method that is recommended by the National Kidney Foundation [25]. The clinical validity of DCE-MRI for the quantification of renal function depends on its agreement with such a reference method.

The objective of this study was twofold: first, to investigate whether DCE-MRI can detect differences and potential adaption in single-kidney parenchymal volume, renal perfusion, and GFR in the remaining kidney of healthy donors compared with nondonors; and, second, to evaluate the validity of the imaging method in terms of agreement between MRI-derived GFR and iohexol GFR in donors.

Fig. 1—Flow diagram shows study design and tests used to measure glomerular filtration rate (GFR). DCE-MRI = dynamic contrast-enhanced MRI.

Fig. 2—Comparison of iohexol glomerular filtration rate (GFR) and MRI-based GFR measurements. A and B, Graphs show iohexol GFR (A) and MRI-based GFR (B) measurements of donors and control subjects (squares). Solid lines indicate mean GFR values, and diamonds show 95% CIs. Outer dashed lines represent mean ± 2 SDs.

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Subjects and Methods

Study Subjects

The institutional review board approved this prospective study, and all participants gave written informed consent. Between October 2013 and September 2014, 20 donors and 20 healthy control subjects were examined as shown in the flow diagram in Figure 1. The inclusion criteria for the donors were stable kidney function corresponding to CKD stage 3B or an estimated GFR of greater than 45 mL/min/1.73 mL/min. The inclusion criteria for the healthy control subjects were normal weight and age of less than 40 years old. The exclusion criteria for the donors were complications in the post-nephrectomy phase and for the control subjects, the use of any prescribed medication. Further, the exclusion criteria for both groups were any acute illness or disease related to a decline in kidney function, such as renal, hypertensive, or vascular disease; previous allergic reactions to any medication, including contrast agents; and any contraindications to MRI according to the MRI safety checklist. Living kidney donors were evaluated for inclusion in a consecutive way based on their scheduled regular annual visits at the nephrology outpatient clinic. DCE-MRI and iohexol GFR testing were performed as supplementary examinations of the donors exclusively for research purposes. In our institution, no imaging follow-up of kidney donors yet exists. Of 24 donors invited to participate in this study, four refused to participate for personal reasons.

The average time interval (± SD) between donor nephrectomy and DCE-MRI and iohexol GFR testing was 9 ± 5 years (range, 2–17 years). Of the 20 donors, nine had undergone the donor surgery 6 years earlier; five, between 7 and 12 years earlier; and six, between 13 and 18 years earlier. The average time gap between DCE-MRI and iohexol GFR testing was 5 ± 2 days (range, 1–8 days).

For practical and ethical reasons, the healthy control subjects were taken from a sample used in a previous study (not published). The living kidney donors and healthy control subjects were recruited independently and were not matched. The healthy control subjects were recruited from local advertisements at the Haukeland University Hospital and University of Bergen campus. Subjects were invited to undergo two identical DCE-MRI examinations and one iohexol GFR test with the aim to evaluate repeatability and accuracy. To prevent interaction of gadolinium and iohexol contrast agents from affecting kidney function, MRI examinations and iohexol GFR tests were performed at least 2 days apart. The average time gap between the first DCE-MRI examination and iohexol GFR test was 5 ± 4 days (range, 2–12 days). Imaging data from the first of two MRI examinations and iohexol GFR measurements were used as data for the healthy control subjects, which represents an overlap of data between the two studies. Details of subject demographic and laboratory data are provided in Table 1.

Iohexol GFR measurements were performed by injecting 5.0 mL of iohexol (300 mg/mL; Omnipaque 300, GE Healthcare) and obtaining a venous blood sample 4 hours later. The iohexol concentration was analyzed using the single-point high pressure liquid chromatography method according to Jacobsson [26]. Estimated GFR (i.e., serum creatinine clearance) was determined using the Chronic Kidney Disease Epidemiology Collaboration equation according to [27].

MRI Technique

DCE-MRI examinations were performed on a 1.5-T scanner (Avanto, Siemens Healthcare) using a standard phased-array coil. A 3D spoiled gradient-echo sequence was performed using the following parameters: TR/TE, 2.36/0.8; flip angle, 20°; matrix, 192 × 192; FOV, 425 × 425 × 90 mm; voxel size, 2.2 × 2.2 × 3.0 mm; and temporal resolution, 2.3 seconds. The generalized autocalibrating partial parallel acquisition factor was 3. The 3D volumes were acquired continuously during a total scanning time of approximately 5 minutes using an oblique coronal slice direction covering the kidney and aorta.

Table 1: Demographic and Laboratory Data for the Donors and Healthy Control Subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Donors</th>
<th>Healthy Control Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Sex (no. of subjects)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Male</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Mean age (y)</td>
<td>51 (38–67)</td>
<td>25 (20–38)</td>
</tr>
<tr>
<td>Mean body surface area (m²)</td>
<td>1.93 (1.67–2.16)</td>
<td>1.77 (1.51–2.00)</td>
</tr>
<tr>
<td>Mean body mass index²</td>
<td>25.7 (17.6–32.7)</td>
<td>22.6 (18.0–27.0)</td>
</tr>
<tr>
<td>Serum creatinine value (µmol/L)</td>
<td>88 ± 11b</td>
<td>70 ± 15b</td>
</tr>
<tr>
<td>Erythrocyte volume fraction</td>
<td>0.42 ± 0.03b</td>
<td>0.41 ± 0.03b</td>
</tr>
<tr>
<td>Mean interval between transplant and renal function assessment (y)</td>
<td>9 (2–17)</td>
<td></td>
</tr>
</tbody>
</table>

Note—Numbers in parentheses are ranges.

*Mean ± SD.

A

B

Fig. 3—Relationship between donor iohexol glomerular filtration rate (GFR) and donor age and time since nephrectomy. A and B, Graphs show relationships between donor iohexol GFR and age (A) and between donor iohexol GFR and time since nephrectomy (B). Numbers by data points (small squares) correspond to unique subject number. Large squares show median iohexol GFR; first quartile (lower dashed line) and third quartile (upper dashed line) GFR values are shown.
DCE-MRI to Quantify Kidney Function and Volume

A repeated breath-hold protocol was used to record image data with minimal impairment from motion. Before the injection of contrast agent, eight baseline volumes were acquired during an 18-second breath-hold phase to obtain a reliable unenhanced signal intensity baseline for the measurement of tracer concentration. A bolus injection of 0.025 mmoL/kg of gadoterate meglumine (Dotarem, Guerbet) was administered at 3 mL/s followed by a 20-mL saline flush through a 20-gauge needle placed in an antecubital vein using an automated power injector (Optistar LE, Mallinckrodt). Seven seconds after the contrast agent injection, during the first pass, the subjects were instructed to hold their breath for 26 seconds. Subsequent instructions for 13-second breath-holds and 26 seconds of free breathing were given during continuous scanning. During the free-breathing intervals, subjects were asked to breathe as shallowly as possible. Subjects received 1 L/min of oxygen through a nasal cannula to ease breathing.

Data Analysis

The DCE-MRI data were exported from the scanner to an external workstation for postprocessing. First, a nonparametric automated registration method, implemented in Matlab (version R2014b, MathWorks) with normalized gradients as the Cost function, was used for kidney motion correction; see [28] for details. Registered data including all time frames were then converted back into DICOM format and were postprocessed using Platform for Research in Medical Imaging (PMI) software (PMI, version 0.4, University of Leeds) [29], which is written in Interactive Data Language (version 6.4, David Stern & ITT Visual Information Solutions), for model-based estimations of renal functional parameters. An operator with 4 years’ experience in renal DCE-MRI analyses performed the pharmacokinetic PMI analyses using default parameters and was blinded to information about estimated GFR and iohexol GFR.

The ROI defining the arterial input function (AIF) was defined semiautomatically on maximum-signal-intensity maps by selecting the 10–15 brightest voxels along the long axis of the aorta, starting just below the orifices of the renal arteries in the midcoronal slice. Parenchymal volumes—excluding extrarenal structures and the renal collecting system—were selected on AUC maps. A scaled gadolinium concentration–time curve ($\hat{S}_t$) from the whole parenchymal volume was fitted to a two-compartment filtration model comprising the following four independent parameters: plasma volume, tubular flow, tubular transit time, and plasma transit time; this step was implemented in PMI [30]. $\hat{S}_t$ was estimated from the signal enhancement using the following equation:

$$\hat{S}_t = S_t - S_0,$$

where $S_0$ is the baseline signal intensity and $S_t$ is the signal intensity at time $t$.

Fig. 3 (continued)—Relationship between donor iohexol glomerular filtration rate (GFR) and donor age and time since nephrectomy. A and B, Graphs show relationships between donor iohexol GFR and age (A) and between donor iohexol GFR and time since nephrectomy (B). Numbers by data points (small squares) correspond to unique subject number. Large squares show median iohexol GFR, first quartile (lower dashed line) and third quartile (upper dashed line) GFR values are shown.

Fig. 4—Comparison of dynamic contrast-enhanced MRI (DCE-MRI)–measured renal blood flow of donors and control subjects. A and B, Graphs show DCE-MRI–measured blood flow as flow rate per minute (mL/min) (A) and as perfusion per 100 mL of renal parenchyma (mL/min/100 mL) (B) in donors and control subjects. Solid lines indicate mean values, and diamonds show 95% CIs. Dashed lines represent mean ± 2 SDs.
Conversion from plasma to blood concentration was performed in PMI by taking the measured erythrocyte volume fraction into account. The kidney perfusion parameters renal blood flow ($F_b$) and renal plasma flow ($F_p$) in units of mL/min/mL were derived from the following two equations:

$$F_b = V_b / T_b,$$

and

$$F_p = V_p / T_p,$$

where $V_b$ and $V_p$ are the blood volume and plasma volume, respectively, and $T_b$ and $T_p$ are the mean transit times (in minutes) of renal blood and renal plasma, respectively. Renal $F_b$ and $F_p$ were further converted to absolute flow (mL/min) by multiplying with the whole kidney volume. GFR was determined as the following product:

$$GFR = F_b \times V_{par},$$

where $F_b$ is the flow into the tubules (mL/min/mL) and $V_{par}$ is the renal parenchymal volume (in milliliters). The filtration fraction represents the proportion of plasma entering the kidneys that is filtered by the glomeruli.

**Statistical Analyses**

Descriptive statistics are given as means and SDs. For comparison of the donor group and the healthy control group, the percentage difference in means is reported. The two-tailed Student $t$ test with independent samples was applied to test for differences in means.

An ANOVA was applied to three different groups categorized by years since donation to test whether time since donation had a significant impact on the renal measurements of donors.

The Pearson correlation coefficient ($r$) was calculated to test the strength of association. A $p$ value of $<0.05$ was considered to indicate statistical significance.

The accuracy of the GFR measurements in donors was summarized as the mean difference (bias) and the limits of agreement between MRI-derived GFR and the reference iohexol GFR. A Bland-Altman plot was drawn for visualization. Absolute agreement between MRI-derived GFR and iohexol GFR was assessed in terms of the intraclass correlation coefficient (ICC) using a two-way random-effects ANOVA model.

To adapt to the recommendations of the National Kidney Foundation [25], we also report accuracy in terms of the percentage of MRI-derived GFR estimates that fell within 10%, 30%, and 50% above or below the iohexol GFR.

**Results**

**Estimates of Total and Single-Kidney Glomerular Filtration Rates in Donors and Healthy Control Subjects**

Demographic and laboratory data for the donors and healthy control subjects are presented in Table 1. DCE-MRI examinations and blood tests were successfully performed in all subjects and were included for analysis. The results are summarized in Table 2. The total iohexol GFR was significantly lower in donors (mean, 84 mL/min; SD, 13) than in the healthy control subjects (mean, 105 mL/min; SD, 10) (two-tailed Student $t$ test, $p > 0.0001$). The distribution of measurements is shown in Figure 2A. By comparison, the MRI-based GFR measurements showed no statistically significant difference ($p = 0.188$) in the total MRI-based GFR measurements between donors (mean, 98 mL/min; SD, 26) and healthy control subjects (mean, 109 mL/min; SD, 25). MRI-based GFR measurements had a considerably larger SD and distribution overlap between the groups compared with the reference iohexol GFR, as shown in Figure 2B.

**Donor Age and Time Since Nephrectomy**

Donor age was negatively correlated with both iohexol GFR ($r = –0.551, p = 0.0117$) and MRI-based GFR ($r = –0.557, p = 0.0107$). The relationship between donor iohexol GFR and age is presented in Figure 3A. A similar age-related decline in glomerular filtration was not found in the healthy control subjects for either the iohexol GFR ($p = 0.3780$) or the MRI-based GFR ($p = 0.5593$). No significant associations were found between iohexol GFR and time since donation, as illustrated in Figure 3B.
Kidney Parenchymal Volume Estimates

A 65% increase in the single-kidney parenchymal volume was measured in donors (mean, 263 mL; SD, 43) compared with healthy control subjects (mean, 159 mL; SD, 20). Accordingly, a 78% increase in single-kidney GFR, a 54% increase in renal blood flow, and a 51% increase in renal plasma flow were found in donors compared with the control group (Table 2). Significant differences in filtration and perfusion estimates between the two groups diminished when parameters were normalized to the renal parenchymal volume (i.e., presented as tubular flow, renal blood flow, and renal plasma flow in units of mL/min/100 mL). Figure 4 illustrates how the measured renal blood flow equalizes between the two groups relative to the renal parenchymal volume. Further, the filtration fractions were determined, and there were no significant differences in filtration fractions between donors (mean, 20%; SD, 4%) and healthy control subjects (mean, 18%; SD, 7%).

Figure 5 shows high Pearson correlation coefficients between renal parenchymal volume and iohexol GFR (r = 0.694, p = 0.0007), estimated GFR (r = 0.764, p < 0.0001), MRI-based GFR (r = 0.658, p = 0.0016), and renal blood flow (r = 0.656, p = 0.0017) in donors.

Agreement Between MRI-Derived Glomerular Filtration Rates and Reference Iohexol Glomerular Filtration Rates

The mean difference between MRI-based GFRs and the reference iohexol GFRs was 14.0 mL/min (SD, 19.5), and the limits of agreement (±2 SDs) ranged from –24.1 to 52.1 mL/min (Fig. 6). The strength of correlation to iohexol GFR was similar for MRI-based GFR (r = 0.75, p < 0.0001) and creatinine level–based estimated GFR (r = 0.78, p < 0.0001) (Table 3). Regardless of the strong Pearson correlation coefficients between the three independent GFR measurement methods, the absolute agreement in the paired GFR measurements, as tested by the ICC, was considerably higher for estimated GFR (ICC = 0.73) than for MRI-based GFR (ICC = 0.49). The Bland-Altman plot illustrates this systematic trend in which lower GFR values provide better accordance between the methods than higher GFR values (Fig. 6).

Significant positive Pearson correlation coefficients were found between the absolute difference of the paired iohexol GFR and MRI-based GFR measurements and both tubular flow (r = 0.648, p = 0.0020) and the physiologic independent parameter of renal blood flow (r = 0.49, p = 0.0293).

According to National Kidney Foundation guidelines, at least 90% of GFR measurements should lie within 30% of the reference method. In our study, 85% (17 donors) of the MRI-based GFRs were within 30% of the reference iohexol GFR values (Fig. 7).

Discussion

The results of this cross-sectional renal DCE-MRI study of 20 living kidney donors and 20 healthy control subjects show a significantly higher renal blood flow, GFR, and renal parenchymal volume in the remaining kidney of donors compared with the single-kidney values of healthy control subjects; these results are compatible with a normal postnephrectomy renal functional reserve [7]. The proportional increases in

TABLE 3: Agreement Between the Measured Total Glomerular Filtration Rate (GFR) in Donors Using Dynamic Contrast-Enhanced MRI Compared With Reference Iohexol GFR and Estimated GFR

<table>
<thead>
<tr>
<th>GFR Methods Being Compared</th>
<th>Total GFR</th>
<th>Mean Difference</th>
<th>Limits of Agreement</th>
<th>ICC</th>
<th>r² (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI-based GFR – iohexol GFR</td>
<td></td>
<td>0.75 (&lt; 0.0001)</td>
<td>14.0</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td>MRI-based GFR – estimated GFR</td>
<td></td>
<td>0.66 (0.0016)</td>
<td>10.3</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Iohexol GFR – estimated GFR</td>
<td></td>
<td>0.78 (&lt; 0.0001)</td>
<td>3.7</td>
<td>0.73</td>
<td></td>
</tr>
</tbody>
</table>

Note—ICC = intraclass correlation coefficient.

a Estimated GFR (serum creatinine clearance) was determined using the Chronic Kidney Disease Epidemiology Collaboration equation according to [27].
b Pearson correlation coefficient.
c Mean ± 2 SDs.
blood flow and GFR yield a filtration fraction in the remaining kidney of donors that is not different from the filtration fraction in a single kidney of control subjects. In addition, when renal blood flow was normalized to parenchymal volume, no significant differences were found between the groups. In donors, MRI-based GFR and renal parenchymal volume were highly correlated with iohexol GFR. Thus, normal physiological long-term regulation of renal blood flow and GFR was observed in healthy living kidney donors up to 17 years after nephrectomy. These results indicate that MRI-based GFR could be a useful GFR imaging biomarker and also that DCE-MRI–based renal parenchymal volume might be used as a surrogate measure for renal function. Furthermore, the combined measurements of renal blood flow and GFR on DCE-MRI have potential for future earlier diagnostic and prognostic assessments of subclinical vascular progressive disease and of the effect of vasoactive medications in the careful follow-up of marginal kidney donors and kidney recipients (e.g., elderly patients and hypertensive patients). Further validation of DCE-MRI is needed to assess the benefit and need to implement this imaging method as part of routine follow-up.

A normal adaptive renal functional response to nephrectomy involves an immediate (<1 week) increase of approximately 40% in renal blood flow and GFR [31, 32]; these changes are sustained through the early postdonation (≈1 year) and late postdonation (≈6 years) periods [33]. The age-related decline in GFR, primarily initiated after the age of 40 years, is shown to be approximately 1 mL/min/y [34–36]. In our study, we found a significant correlation between donor age and iohexol GFR. However, no such correlation was found between time since donation and iohexol GFR, supporting findings of a normal filtration fraction.

In general, little is known about the long-term effects of kidney donation on donor renal function compared with the short-term effects, and MRI research on this issue is scarce. Our DCE-MRI results in living kidney donors are consistent with DCE-MRI results showing renal functional adaptation in the contralateral kidney after nephrectomy for renal cancer: Su et al. [37] reported a 43% and 66% correlational increase in renal blood flow and parenchymal volume, respectively. Adaptive renal response in living kidney donors has recently been studied using other MRI techniques, such as ASL [7], DWI [2], and unenhanced MRI [8]. Cutajar et al. [7] used ASL and reported increases in donor renal volume (range, 10–29%), renal plasma flow (range, 0–33%), and GFR measured using $^{51}$Cr–ethylenediamine tetaacetic acid (range, 24–75%) 1 year after nephrectomy. Consistent with our findings, Cutajar and co-workers observed no difference in renal plasma flow or GFR when parameters were normalized per 100 g (100 mL) of parenchymal volume. Eisenberger and colleagues [2] reported early adaptions in the remaining kidney of donors in terms of reduced apparent diffusion coefficient values and increased estimated GFR and found no significant correlation between the two methods. Song et al. [8] recently reported that an immediate

Fig. 5 (continued)—Correlation plots between renal parenchymal volume (y-axis) and glomerular filtration rates (GFRs) and renal blood flow in donors. A–D: Correlation plots between renal parenchymal volume (y-axis) and iohexol GFR (A), estimated GFR (B), MRI-based GFR (C), and renal blood flow (D). Numbers by data points (squares) correspond to unique subject number. Dashed lines indicate 95% level bivariate normal density ellipsoids of linear correlation. Plus signs indicate ellipsoid centers.
increase of 24% (mean) in renal parenchymal volume shown on unenhanced MRI was significantly correlated with estimated GFR.

Subject age, time since kidney donation, and general health status could influence renal function, and variations in sample characteristics between studies could complicate direct comparison of results. Furthermore, comparing functional characteristics across different MRI techniques (e.g., DCE-MRI, ASL, and DWI) introduces challenges due to inherent differences in the properties of the MRI signals. As for ASL-derived renal plasma flow measurements (range, 190–312 mL/min) in living kidney donors [7], a considerable difference in range was found compared with those derived from DCE-MRI (range, 310–696 mL/min). The lack of non-invasive reference standards for measuring renal plasma flow and renal blood flow complicates direct comparisons.

Strong correlations between MRI-derived GFR and parenchymal volume and between MRI-derived GFR and the reference iohexol GFR emphasize the clinical value of DCE-MRI. Strong correlations between MRI-based GFR and reference methods have previously been reported [16, 18, 38]. However, evidence of their absolute agreement is less documented. Our results indicate that achieving good accuracy in MRI-based GFR estimates is still challenging, as expressed by the lower ICC value and wider limits of agreement than those found between iohexol GFR and estimated GFR (Table 3). Higher bias at higher GFR values (Fig. 6) may be explained in part by irregularities in signal intensity-to-concentration conversion due to potential T2* effects when assuming a linear relationship at all gadolinium concentrations. However, the effect of T2* weighting was reduced by using a short TE and a low contrast agent dose but needs to be investigated further. All steps from acquisition to pharmacokinetic modeling would influence the precision of renal functional measurements. Further validation of DCE-MRI is needed to assess the benefit and need to implement this imaging method as part of routine follow-up.

The close relationship between renal parenchymal volume and renal function has been described in the literature with regard to the use of several imaging techniques, such as unenhanced MRI [8, 39], CT [24, 40], and ultrasound [41]. Physiologically, the compensatory hypertrophy in the remaining kidney of donors is associated with an increase in both glomerular corpuscular and glomerular capillary volumes [33, 42]. Performing parenchymal volume estimations using DCE-MRI would probably reflect more precisely the adaptive functioning parenchyma than using unenhanced techniques. However, using renal volume as a surrogate measure of renal function would not reflect other causes of renal functional changes than volume, and the clinical use of this surrogate measure should be used with this limitation in mind.

Our study has several limitations. Besides a small study cohort, the study setup involved subject samples not matched by age, and the donors were older than the control subjects. Because we do not have longitudinal data on renal function in the donors, the individual renal reserve and absolute renal reserve in the remaining kidney are not measurable. Moreover, a potential selection bias is present because only healthy renal donors are included, thus reducing the generalizability of our results to living kidney donors. Further research on the clinical value of DCE-MRI in living kidney donors should focus on longitudinal studies including the pre- and postnephrectomy stages.

In conclusion, the findings in our study show that DCE-MRI can be used to measure structural and functional differences in the single kidney of donors and healthy control subjects. Donors showed significantly higher single-kidney renal blood flow and GFR than control subjects, and these changes were accompanied by an increase in renal parenchymal volume. Consistent with an expected renal reserve after nephrectomy, a normal filtration fraction comparable to that of healthy control subjects was measured in donors up to 17 years after nephrectomy. Moreover, a strong correlation was found between MRI-based GFR and iohexol GFR. However, MRI-based GFR achieved moderate absolute agreement with iohexol GFR, indicating a need for further validation of the DCE-MRI method. Providing both clinically relevant measures and joint access to structural and functional measures, DCE-MRI emerges as a valuable tool for individualizing clinical workup and characterizing potential early kidney damage in living kidney donors.

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References


