



HAL
open science

Predictive factors of glomerular filtration rate loss associated with living kidney donation: a single-center retrospective study

Arthur Orioux, Antonin Bouchet, Alice Doreille, Liliana Paslaru, Marine Livrozet, Jean-Philippe Haymann, Nacera Ouali, Laurent Mesnard, Emmanuel Letavernier, Pierre Galichon

► To cite this version:

Arthur Orioux, Antonin Bouchet, Alice Doreille, Liliana Paslaru, Marine Livrozet, et al.. Predictive factors of glomerular filtration rate loss associated with living kidney donation: a single-center retrospective study. *World Journal of Urology*, 2022, 40 (9), pp.2161-2168. 10.1007/s00345-022-04019-x . hal-04052076

HAL Id: hal-04052076

<https://hal.science/hal-04052076v1>

Submitted on 11 Apr 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License



Predictive factors of glomerular filtration rate loss associated with living kidney donation: a single-center retrospective study

Arthur Orieux¹ · Antonin Bouchet^{2,3} · Alice Doreille² · Liliana Paslaru⁴ · Marine Livrozet^{1,5} · Jean-Philippe Haymann^{1,5} · Nacera Ouali² · Laurent Mesnard^{1,2} · Emmanuel Letavernier^{1,5} · Pierre Galichon^{1,2} 

Received: 23 October 2021 / Accepted: 16 April 2022 / Published online: 20 May 2022
© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2022

Abstract

Purpose Living kidney donors (LKD) partially compensate the initial loss of glomerular filtration rate (GFR), a phenomenon known as renal functional reserve (RFR). RFR is reduced in the elderly, a population with increased prevalence of chronic kidney disease. We hypothesized that the selected, healthy population of LKD, would specifically inform about the physiological determinants of the RFR and studied it using measured GFR (mGFR).

Methods We retrospectively analyzed pre-donation and post-donation mGFR in 76 LKD from Tenon Hospital (Paris, France) between 2002 and 2018. In addition to GFR measurements, we collected pre-donation morphologic parameters, demographic data, and kidney volumes.

Results Mean pre-donation mGFR was 90.11 ± 12.64 mL/min/1.73 m² and decreased to 61.26 ± 9.57 mL/min/1.73 m² 1 year after donation. Pre-donation mGFR correlated with age ($p=0.0003$), total kidney volume ($p=0.0004$) and pre-donation serum creatinine ($p=0.0453$). Pre-donation mGFR strongly predicted 1-year post-donation mGFR. Mean RFR (increase in GFR of the remnant kidney between pre-donation and post-donation) was $36.67 \pm 16.67\%$ 1 year after donation. In the multivariate linear model, RFR was negatively correlated to total kidney volume ($p=0.02$) but not with age or pre-donation serum creatinine.

Conclusions We found that pre-donation mGFR decreases with age and identified low total kidney volume as a predictor of RFR in healthy individuals. This suggests an adaptative and reversible decrease in kidney function rather than age-related damage. Older subjects may have reduced metabolic requirements with subsequent reduction in glomerular filtration and kidney volume and preserved RFR. Therefore, low GFR in older subjects should not preclude kidney donation.

Keywords Kidney transplantation · Living kidney donation · GFR decrease risk stratification · Glomerular hyperfiltration · Renal functional reserve

Arthur Orieux, Antonin Bouchet and Alice Doreille contributed equally.

✉ Pierre Galichon
pierre.galichon@aphp.fr

¹ Sorbonne Université, UMR_S 1155, INSERM, Tenon Hospital, Paris, France

² Department of Nephrology, Assistance Publique-Hôpitaux de Paris, Tenon Hospital, Sorbonne Université, Paris, France

³ Claude Bernard University Lyon I, Lyon, France

⁴ Department of Radiology, Assistance Publique-Hôpitaux de Paris, Tenon Hospital, Sorbonne Université, Paris, France

⁵ Department of Physiology, Assistance Publique-Hôpitaux de Paris, Tenon Hospital, Sorbonne Université, Paris, France

Abbreviations

| | |
|---------|---|
| BMI | Body mass index |
| BSA | Body surface area |
| CKD-Epi | Chronic kidney disease-epidemiology collaboration |
| CKD | Chronic kidney disease |
| CT | Computerized tomography |
| eGFR | Estimated glomerular filtration rate |
| ESRD | End-stage renal disease |
| GFR | Glomerular filtration rate |
| IQR | Interquartile range |
| LKD | Living kidney donors |
| mGFR | Measured glomerular filtration rate |
| RFR | Renal functional reserve |
| SD | Standard deviation |

Introduction

Kidney transplantation is the standard treatment for end-stage renal disease (ESRD) and is superior to dialysis in survival, quality of life, and health economics [1–3]. In addition, kidney transplantation from living kidney donors (LKD) is associated with better graft and patient survival rates [4]. Indeed, LKD are rigorously selected (absence of renal pathology and few renal injury factors) before donation to reduce the risk of chronic kidney disease (CKD). Furthermore, with the global aging of the populations in developed countries, ESRD patients and their potential donors are older.

Renal function assessed by creatinine clearance or glomerular filtration rate (GFR) decreases linearly with age [5, 6]. However, this age-related decline is independent of renal histologic changes [7], and some elderly patients do not have a kidney function alteration [8]. Moreover, renal volume decreases with age, including inpatients without risk factors for kidney disease (hypertension, diabetes) [9]. In the elderly, renal function and renal blood flow are reduced compared to younger ones, but the serum creatinine and urea concentration can be identical. Renal functional reserve (RFR) is defined as the capacity of the kidney to increase GFR in response to physiological or pathological stress (as for unilateral nephrectomy). RFR assessed in the short term is conserved but reduced in the healthy elderly population [10, 11].

Previous studies have shown that, after an initial increase in serum creatinine, LKD develop a RFR by undergoing compensatory kidney hypertrophy, thus improving their renal function over circa 3 months after donation [12–14].

We hypothesized that a selected population of LKD (healthy patients) would allow studying the physiological determinant of the RFR, excluding the effect of coexisting kidney diseases. Therefore, the main objective of this study was to assess predictive factors of RFR in a healthy LKD population of diverse ages.

Materials and methods

Study design and patients

This retrospective cohort study was carried out in Tenon hospital (Paris) from March 2002 to September 2018. During this period, we screened all LKD patients. We excluded patients without a measure of pre-donation or post-donation and those whose mGFR 1 year after donation were unavailable.

Collected data

Collected variables of interest were mGFR, estimated GFR (eGFR) with Chronic Kidney Disease–Epidemiology Collaboration (CKD-Epi) formula [15] at every available time-point, anthropometric data, pre-donation kidney volumes, pre-donation risk factors for renal failure according to the 2017 KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors [16]. In addition, hypertension was defined as high blood pressure > 140/90 mmHg and obesity as a body mass index (BMI) > 30 kg/m².

GFR measurement

GFR was measured with radioactive ⁵¹Cr-EDTA renal clearance technique in the Department of Physiology in Tenon hospital as described previously [17, 18]. Briefly, 1.8 to 3.5 MBq of ⁵¹Cr-EDTA were injected intravenously as a single bolus. Average renal ⁵¹Cr-EDTA clearance was determined over 5 to 6 consecutive 30 min clearance periods.

The renal functional reserve (RFR) was expressed in percentage, and calculated with the following formula:

$$\text{RFR(\%)} = 100 \times \frac{[\text{mGFR}_{\text{post}} - (0.5 \times \text{mGFR}_{\text{pre}})]}{0.5 \times \text{mGFR}_{\text{pre}}}$$

mGFR_{pre}: pre-donation measured GFR (mL/min/1.73 m²), mGFR_{post}: 1-year post-donation measured GFR (mL/min/1.73 m²).

Serum creatinine and mGFRs were measured before donation in LKD during the pre-transplant assessment carried out a few months before renal transplantation (maximum 6 months). mGFRs assessments were performed 1 year after donation in LKD (between 6 and 18 months after donation).

Kidney volume assessment

Pre-donation computerized tomography (CT) images on arterial phase were used to estimate kidney volumes, with a semi-automated volumetric segmentation tool based on tissue density (Segmentation Management module, Carestream software, Carestream Health Inc. Rochester, NY, USA). Dr. Liliana Paslaru (medical doctor in radiology) and Alice Doreille (resident in nephrology) performed the kidney volume measurements. The method for kidney measurement is detailed in Supplemental Fig. 1.

Statistical analyses

Statistical analysis was carried out using Graphpad Prism 9.0 for Mac (Graphpad Software, San Diego, California, USA). Continuous variables were tested for normality

(Shapiro Wilk test) and expressed as mean \pm standard deviation (SD) or as median with interquartile range (IQR) according to distribution. Categorical variables were expressed as numbers (percentage of total). Variables were compared using student *t* test or Wilcoxon–Mann–Whitney test (continuous variables) and χ^2 or Fisher’s exact test (categorical variables) depending on group size and distribution. The multivariate analysis was carried out using linear regression. Interactions between independent variables were checked using the Pearson correlation test for quantitative variables. Test results with *p* values < 0.05 were considered significant (double-sided).

Results

Patients

Hundred and twenty adult patients donated a kidney in Tenon Hospital from March 2002 to September 2018 (Fig. 1). Thirty-one out of 120 (26%) patients were excluded because of the absence of pre-donation or post-donation mGFR. Thirteen out of 89 (15%) patients were excluded, because no available post-donation mGFR at 1 year. Finally, we included 76 LKD. The nephrectomy was performed by open surgery until September 2014 and by laparoscopy thereafter.

Living kidney donor’s characteristics (Table 1)

From 76 LKD, the mean age was 49 ± 10 years, 24 out of 76 (32%) patients were men, and 17 (22%) were black, mean BMI was 26.8 ± 4.4 kg/m².

In this cohort of healthy patients, risk factors for kidney disease were rare: only 6 out of 76 (8%) patients suffered

from hypertension. Microalbuminuria and a history of kidney stones were rare (7 and 3%, respectively). No LKD had diabetes or previous microscopic hematuria. Some patients presented cardiovascular risk factors: dyslipidemia, obesity, and tobacco use (37, 22, and 22%, respectively).

Mean donated kidney volume was 162.4 ± 26.6 mL and mean remaining kidney volume 159.5 ± 26.1 mL, the corresponding percentage from total kidney volume were 50.4 and 49.6%, respectively.

Pre-donation mGFR was correlated with age, kidney volume, and pre-donation serum creatinine

Mean pre-donation mGFR was 90.11 ± 12.64 mL/min/1.73 m², with heterogeneous distribution (65.71 to 134.81 mL/min/1.73 m²) (Supplemental Fig. 2). We found that pre-donation mGFR was linearly correlated with age and total kidney volume in these healthy subjects but not with serum creatinine (Fig. 2A–C).

A linear regression model was established to identify pre-donation mGFR predictor factors, including morphologic parameters that are constantly available in potential kidney donors (Table 2). In multivariate analysis, association of mGFR with age [β coefficient: -0.52 , 95% CI (-0.79 ; -0.25), $p=0.0003$], total kidney volume [β coefficient: 0.10 , 95% CI (0.05 ; 0.15), $p=0.0004$] and pre-donation serum creatinine [β coefficient: -0.17 , 95% CI (-0.34 ; -0.004), $p=0.0453$] were significant.

mGFR 1 year after donation

One year after donation, the mean mGFR was 61.26 ± 9.57 mL/min/1.73 m² and half of the patients had a mGFR ≤ 60 mL/min/1.73 m² (Supplemental Fig. 3). In univariate analysis, pre-donation mGFR was significantly associated with post-donation mGFR (β coefficient: 0.49 , $p < 0.0001$) (Supplemental

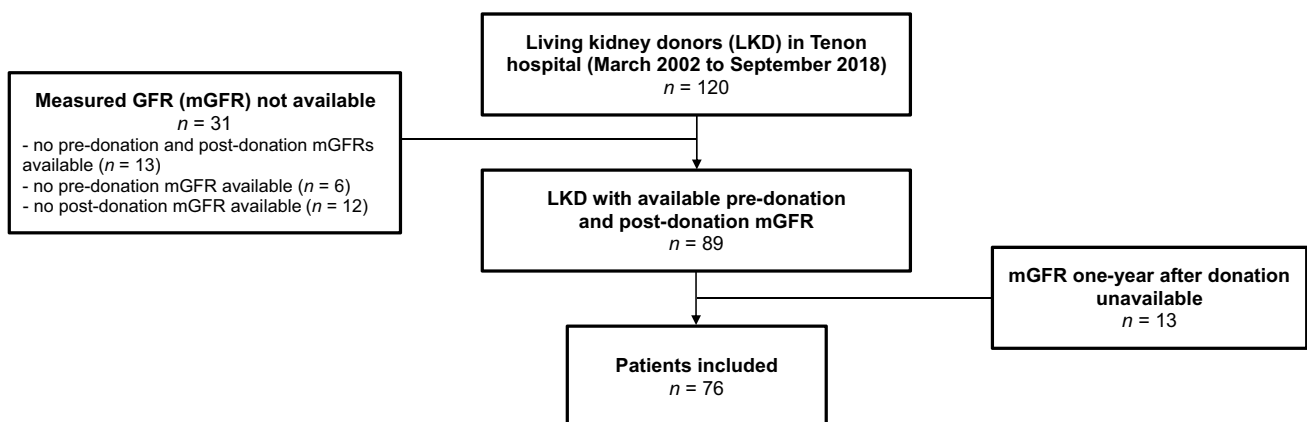


Fig. 1 Flowchart LKD living kidney donors, mGFR measured glomerular filtration rate

Table 1 Living kidney donors characteristics ($n=76$)

| | All patients $n=76$ | < 50 years $n=37$ | ≥ 50 years $n=39$ |
|--|---------------------|-------------------|------------------------|
| Demographic baseline characteristics | | | |
| Age (years) | 49 \pm 10 | 41 \pm 6 | 59 \pm 5 |
| Male sex, N . (%) | 24 (32) | 13 (35) | 11 (28) |
| Black ethnicity, N . (%) | 17 (22) | 12 (32) | 5 (13) |
| Body mass index (BMI, kg/m ²) | 26.8 \pm 4.4 | 26.8 \pm 4.2 | 26.8 \pm 4.6 |
| Body surface area (BSA, m ²) | 1.81 \pm 0.18 | 1.81 \pm 0.19 | 1.81 \pm 0.17 |
| Kidney volumes of LKD ^a | | | |
| Total kidney volume (mL) | 321.9 \pm 49.4 | 317.6 \pm 43.9 | 326.3 \pm 54.9 |
| Donated kidney volume (mL) | 162.4 \pm 26.6 | 160.6 \pm 24.9 | 164.3 \pm 28.5 |
| Corresponding percentage from total kidney volume (%) | 50.4 | 50.5 | 50.3 |
| Remaining kidney volume (mL) | 159.5 \pm 26.1 | 157.1 \pm 21.42 | 162 \pm 30.5 |
| Corresponding percentage from total kidney volume (%) | 49.6 | 49.5 | 49.7 |
| Kidney failure risk factors of LKD | | | |
| Dyslipidemia, N . (%) | 28 (37) | 7 (19) | 21 (54) |
| Tobacco use, N . (%) | 17 (22) | 13 (35) | 4 (10) |
| Obesity (BMI > 30 kg/m ²), N . (%) | 17 (22) | 8 (22) | 9 (23) |
| Hypertension, N . (%) | 6 (8) | 1 (3) | 5 (13) |
| Kidney stones, N . (%) | 5 (7) | 0 (0) | 5 (13) |
| Microalbuminuria > 3 mg/mmol, N . (%) | 2 (3) | 1 (3) | 1 (3) |
| Microscopic hematuria > 10/mm ³ , N . (%) | 0 (0) | 0 (0) | 0 (0) |
| Diabetes, N . (%) | 0 (0) | 0 (0) | 0 (0) |
| Glomerular filtration rate (GFR) assessment | | | |
| Pre-donation eGFR (CKD-Epi, mL/min/1.73 m ²) | 94.06 \pm 15.75 | 109.7 \pm 14.83 | 90.11 \pm 12.64 |
| Pre-donation mGFR (mL/min/1.73 m ²) | 90.11 \pm 12.64 | 95.18 \pm 12.59 | 85.3 \pm 10.79 |
| Post-donation mGFR (mL/min/1.73 m ²) | 61.26 \pm 9.57 | 65.44 \pm 9.55 | 57.29 \pm 7.82 |
| RFR (%) | 36.67 \pm 16.67 | 38.98 \pm 19.96 | 37.76 \pm 16.40 |

BMI body mass index, BSA body surface area, mGFR measured glomerular filtration rate, eGFR estimated glomerular filtration rate, RFR renal functional reserve was expressed in percentage

^a $n=59$ ($n=30$ patients for < 50 years and $n=29$ for ≥ 50 years)

Fig. 4). Mean RFR was $36.67 \pm 16.67\%$ and frequency distribution histograms revealed a large heterogeneity (7.39 to 101.05%) (Supplemental Fig. 5).

RFR was correlated with kidney volume but not with age or pre-donation serum creatinine

In univariate linear model, only total kidney volume [β coefficient: -0.11 , 95% CI (-0.19 ; -0.02), $p=0.0181$] was a significant predictive factor for RFR (Fig. 2D). Age was not associated with RFR [β coefficient: 0.009 , 95% CI (-0.36 ; 0.38), $p=0.96$] (Fig. 2E), nor was serum creatinine [β coefficient: 0.20 , 95% CI (-0.06 ; 0.47), $p=0.13$] (Fig. 2F).

When tested in a multivariate model, total kidney volume was the only remaining predictive factor for RFR [β coefficient: -0.05 , 95% CI (-0.10 ; -0.01), $p=0.016$] (Table 3). Neither age nor pre-donation serum creatinine was significantly associated with RFR.

Discussion

In this study, pre-donation mGFR was correlated with age, kidney volume and pre-donation serum creatinine. Moreover, 1-year post-donation mGFR is strongly predicted by pre-donation mGFR. RFR was correlated with total kidney volume but not with age or pre-donation serum creatinine.

Pre-donation mGFR is the gold standard for evaluating kidney function and the main parameter considered by the nephrologist to assess eligibility for kidney donation. Correctly assessing pre-donation GFR is essential in a donor risk stratification strategy, because once major cardiovascular or CKD risk factors are eliminated or minimized, it is the only parameter left to guide the decision. We confirmed that renal function prior to kidney donation (assessed by pre-donation mGFR) in LKD, decreases linearly with age, total kidney volume and pre-donation serum creatinine [19].

At 1 year, we reported an approximately 30 mL/min/1.73 m² GFR decrease (37% increase of RFR). This

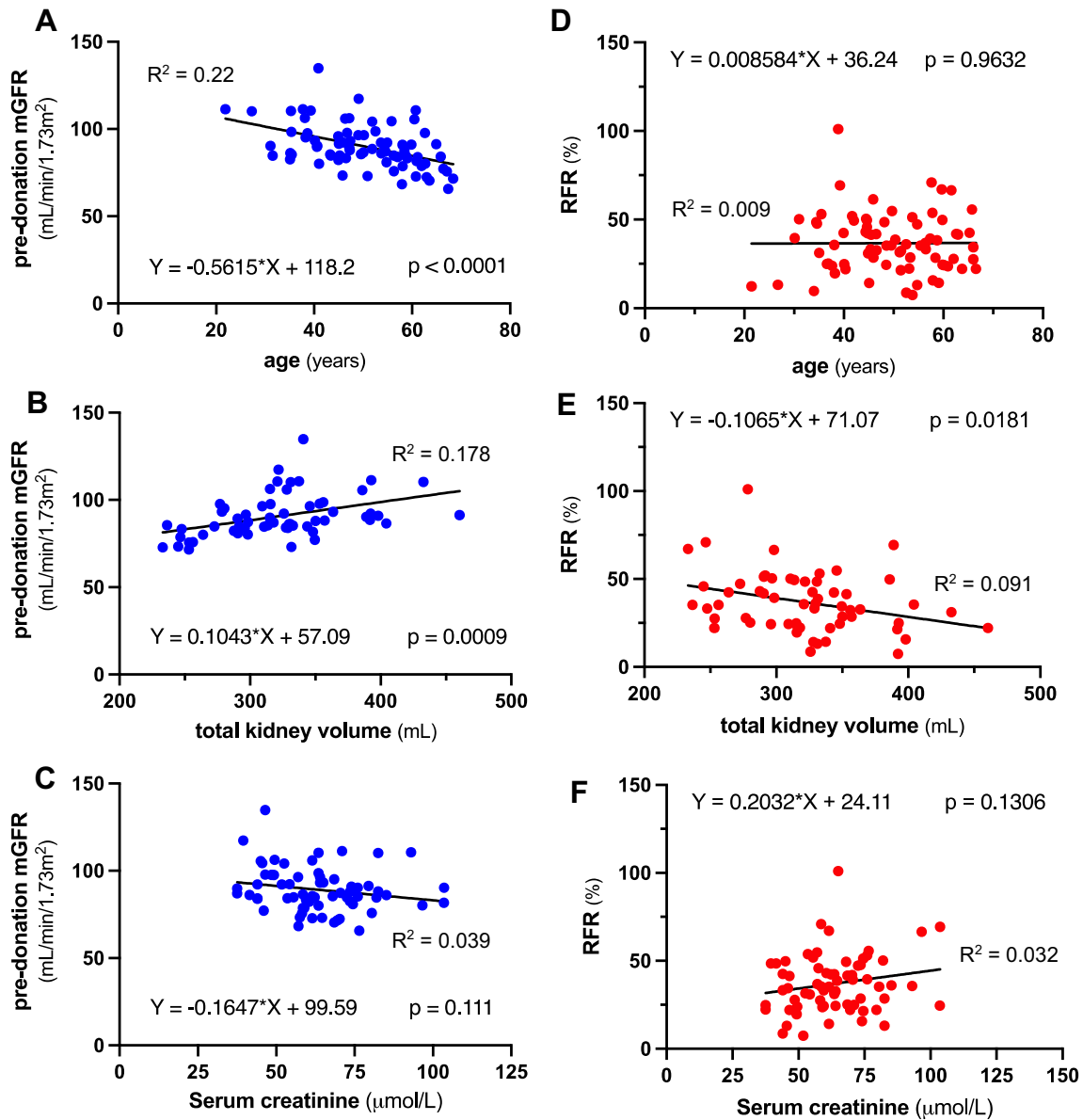


Fig. 2 Simple linear regression of pre-donation mGFR (A, B, C) and RFR (D, E, F). *mGFR* measured glomerular filtration rate, *RFR* renal functional reserve was expressed in percentage, R^2 R-squared

Table 2 Linear regression model for pre-donation mGFR

| Pre-donation characteristics | Univariate analysis | | | Multivariate analysis | | | |
|--|---------------------|----------------|-------------------|-----------------------|----------------|----------------|--------------------|
| | Coefficient | Standard error | <i>p</i> value | Coefficient | Standard error | <i>p</i> value | 95% CI coefficient |
| Age (years) | -0.392 | 0.086 | <0.0001 | -0.520 | 0.134 | 0.0003 | (-0.79; -0.25) |
| Male sex | 0.006 | 0.004 | 0.176 | | | | |
| Black ethnicity | 0.003 | 0.004 | 0.400 | | | | |
| Body mass index (kg/m ²) | -0.203 | 0.040 | 0.616 | | | | |
| Pre-donation serum creatinine (μmol/L) | -0.234 | 0.145 | 0.111 | -0.172 | 0.084 | 0.045 | (-0.34; -0.004) |
| Total kidney volume (mL) | 1.694 | 0.485 | 0.0009 | 0.100 | 0.027 | 0.0004 | (0.05; 0.15) |

Significant *p* values (< 0.05) are in bold

Table 3 Linear regression model for RFR

| Pre-donation characteristics | Univariate analysis | | | Multivariate analysis | | | |
|--|---------------------|----------------|----------------|-----------------------|----------------|----------------|--------------------|
| | Coefficient | Standard error | <i>p</i> value | Coefficient | Standard error | <i>p</i> value | 95% CI coefficient |
| Age (years) | 0.009 | 0.147 | 0.954 | − 0.073 | 0.113 | 0.52 | (− 0.29; 0.15) |
| Male sex | − 0.006 | 0.006 | 0.342 | | | | |
| Black ethnicity | − 0.005 | 0.006 | 0.439 | | | | |
| Body mass index (kg/m ²) | − 0.007 | 0.061 | 0.916 | | | | |
| Pre-donation serum creatinine (μmol/L) | 0.343 | 0.224 | 0.131 | 0.095 | 0.071 | 0.18 | |
| Total kidney volume (mL) | − 1.769 | 0.727 | 0.018 | − 0.055 | 0.022 | 0.016 | (− 0.10; − 0.01) |

Significant *p* values (< 0.05) are in bold

result is consistent with already published data [20–22]. Furthermore, 1-year post-donation mGFR was highly correlated with pre-donation mGFR, justifying the importance of pre-donation GFR measurement in donor risk stratification in transplantation centers. Contrary to absolute post-donation mGFR value, RFR more accurately reflects renal function gain after donation, since absolute GFR gain is expressed as a percentage of its baseline value. Thus, for example, GFR does not decrease by 50% after unilateral nephrectomy, whereas 50% of the nephron mass was indeed removed. Instead, a compensatory increase in glomerular filtration of the remaining kidney results in a limited GFR decrease to approximately 70% of its baseline value [20]. This phenomenon is explained by the concept of RFR [23], defined as the renal capacity to increase GFR from baseline to a maximum value in situations of physiological or pathological stimuli (unilateral nephrectomy).

Rather than measuring short-term RFR (e.g., using amino acid infusions to cause hyperfiltration), we studied RFR in the long term, taking into account hypertrophy as well as hyperfiltration, which is more relevant to the evaluation of donation outcomes. In that perspective, predicting impaired long-term RFR might be very helpful in donor candidates' risk stratification. In our population, a multivariate linear model identified total kidneys volume as a predictive factor of low RFR. Age and serum creatinine pre-donation were not associated with RFR. The association of RFR with lower kidney volumes suggests that they have a higher potential for compensatory hypertrophy. In a sensitivity analysis, we found that the association between kidney volume and RFR is strongest in patients aged ≥ 50 , supporting this hypothesis (Supplementary Figs. 6, 7). Serum creatinine was a poor predictor of pre-donation mGFR, suggesting that variations in serum creatinine might depend on creatinine production (muscular mass, age, and ethnicity) rather than glomerular filtration in these healthy patients, and that serum creatinine should not be used as a marker of renal function in this population.

Although pre-donation GFR was the only factor predicting post-donation GFR, our results also indicate that healthy patients with a low kidney volume have a higher RFR than patients with a higher kidney volume.

Gaillard et al. (2018) recently demonstrated that older patients with a low GFR (< 90 mL/min/1.73 m²) were perfectly suitable donor candidates by introducing a new concept, the lifetime standardized renal reserve [24]. The authors proposed a theoretical formula to estimate an age of ESRD (GFR < 15 mL/min/1.73 m²) for donors with a 5-year post-donation measured GFR considering a constant age-related annual GFR decline. However, GFR decrease is not systematic and inconstant across age, challenging the concept of lifetime RFR. In our healthy LKD population, we observed that the age-related decline in GFR is associated with a lower relative decrease after donation, confirming previous studies showing that older donors might have a conserved RFR. Lam et al. (2020) recently observed that after a GFR drop due to kidney donation, eGFR increases (attributed to compensatory hypertrophy) up to 5-year post-donation [25]. Therefore, after a sudden drop in renal function due to kidney donation, we hypothesize that in this healthy population, the RFR recruitment of a suddenly reduced renal volume would halt the progressive decline in renal function accompanying the age-related decrease in metabolism (Fig. 3). This stabilization of GFR with age would be maintained until the GFR exceeds metabolic requirements. Especially in older patients, the RFR is thus useful to complement pre-donation mGFR to predict the consequence of kidney donation.

Our study has several limitations. The major one resides in its retrospective nature. Indeed, one-third of the 120-screened donor could not be included because of missing data. In addition, the limited number of patients ($n = 76$) from a single center may have caused a lack of power, although the enrollment was exhaustive. Because of the long time span of this study some changes in the donation procedure may have occurred. For example the procedure

changed from open surgery to laparoscopy in 2014. However, comparing donations performed before and after this change, we found no difference in donor age, kidney volume, or renal functional reserve.

Assessing RFR as a complementary tool to mGFR in LKD risk stratification strategy is an exciting concept that has been evaluated in a few studies so far, yet with disappointing results. A pilot study by Spinelli A. et al. (2017) with seven pairs of LKD and recipients reported a mean pre-donation RFR around 30 mL/min/1.73 m² (assessed by oral protein load test) that decreased 3 years after donation to 7.9 and 14.9 mL/min/1.73 m², respectively in donors and recipients, but did not evaluate its impact on post-donation GFR [26]. A Dutch cohort study by van Londen et al. (2018) used dopamine-infusion to measure pre-donation and post-donation RFR in 937 LKD and compared those data with GFR changes [12]. Mean baseline RFR was 10 mL/min/1.73 m² and decreased to 3 mL/min/1.73 m² 3 months after donation. Dynamic tests to assess RFR only inform on potential hemodynamic adaptation but overlook the potential for compensatory hypertrophy. In our study, RFR was negatively correlated with pre-donation mGFR and the total kidney volume. It comforts our hypothesis that high pre-donation GFR might correspond to patients with glomerular hyperfiltration and renal hypertrophy and low RFR or that a relatively low pre-donation mGFR in healthy individuals is not pathological (elderly patients with lower metabolic requirements, for example) and is associated with a preserved potential for

compensatory renal hypertrophy, translating into a lesser decrease in GFR after donation for these patients and, therefore, a highest RFR. It would be interesting to relate RFR with the compensatory hypertrophy post-kidney donation in our study, but CT scans after donation were not available.

Low kidney volume may have very different implications in other populations. It is well known that patients with end stage fibrotic chronic kidney disease frequently have smaller kidneys. Other parameters are needed to distinguish between age-related and pathological reduction in kidney size, especially for the assessment of deceased donors for whom renal risk factors are frequently reported.

Apart from excluding preexisting kidney disease, the current LKD selection strategy allows predicting the 1-year post-donation GFR from the pre-donation mGFR. Although being generally effective, this restrictive strategy (“the higher GFR, the better”) does not take every patient’s characteristics into accounts, such as age and kidney volume. It might select patients with glomerular hyperfiltration with an increased risk of significant GFR loss while abusively excluding healthy donor candidates with low mGFR but with high RFR. RFR estimation base on mGFR and kidney volume may be a good indicator of the kidney’s capacity to compensate for nephron loss.

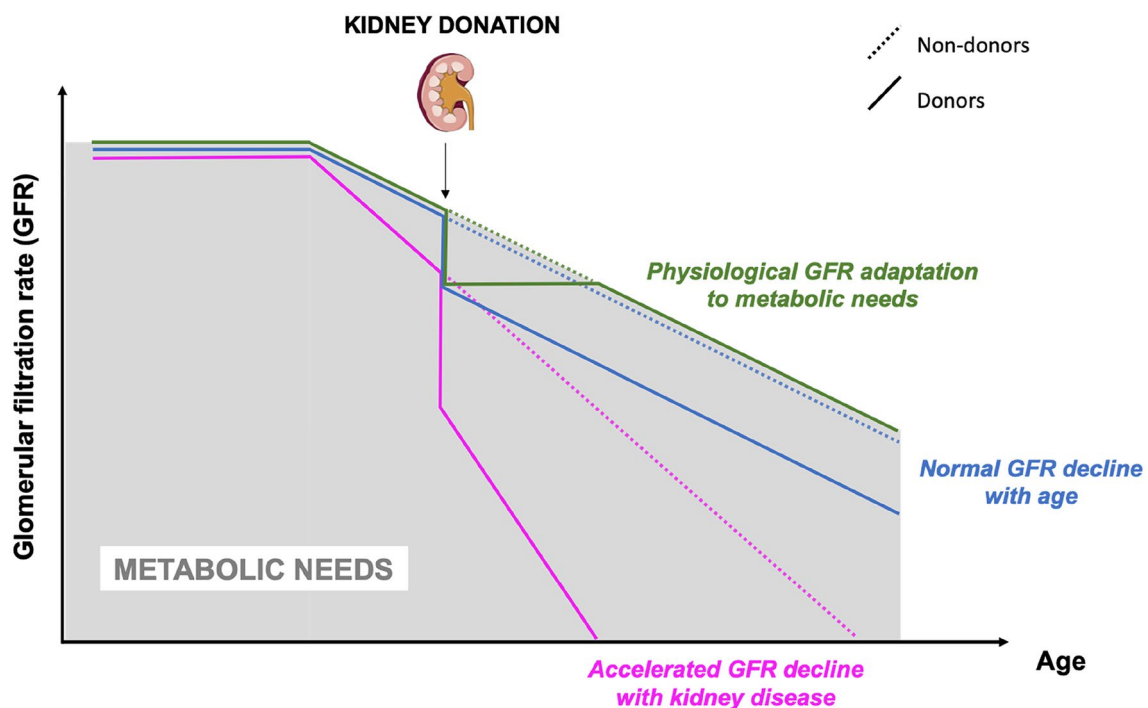


Fig. 3 Schematic representation of metabolic needs according to age

Conclusion

This study found that pre-donation mGFR decreases with age in living kidney donation candidates. Although pre-donation mGFR is strongly correlated with post-donation mGFR, we identified low total kidney volume as a predictor of long-term RFR in these healthy individuals. This suggests an adaptative and reversible decrease in kidney function rather than age-related damage. Older subjects may have reduced metabolic requirements with subsequent reduction in glomerular filtration and kidney volume. Therefore, low GFR in older subjects should not preclude kidney donation and should also be assessed in terms of predicted renal functional reserve.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00345-022-04019-x>.

Author contributions Conceptualization and methodology: AO, AB, ML, PG. Data acquisition: AB, AD, ML, PG, LP, NO, EL. Data interpretation: AO, AB, ML, PG. Writing—original draft: AO, AB, PG. Writing—review and editing: AO, AB, AD, ML, JH, EL, LM, PG.

Funding Pierre Galichon was supported by a grant from ATIP-Avenir 2019.

Declarations

Conflict of interest The authors declared that there is no conflict of interest.

Ethical approval Our retrospective study was conducted solely on already available data. In compliance with the French legislation, this research does not involve a human person, thus neither formal consent nor approval by an institutional review board is needed (Jardé Act and Law No. 78-17 of 6 January 1978 relating to computers, files and freedoms).

References

- Wolfe RA et al (1999) Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 341:1725–1730
- Tonelli M et al (2011) Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes: systematic review of kidney transplantation. *Am J Transplant* 11:2093–2109
- Laupacis A et al (1996) A study of the quality of life and cost-utility of renal transplantation. *Kidney Int* 50:235–242
- Hariharan S et al (2000) Improved graft survival after renal transplantation in the United States, 1988 to 1996. *N Engl J Med* 342:605–612
- Rowe JW, Andres R, Tobin JD, Norris AH, Shock NW (1976) The effect of age on creatinine clearance in men: a cross-sectional and longitudinal study. *J Gerontol* 31:155–163
- Schaeffner ES et al (2012) Two novel equations to estimate kidney function in persons aged 70 years or older. *Ann Intern Med* 157:471
- Rule AD (2010) The association between age and nephrosclerosis on renal biopsy among healthy adults. *Ann Intern Med* 152:561
- Lindeman RD, Tobin J, Shock NW (1985) Longitudinal studies on the rate of decline in renal function with age. *J Am Geriatr Soc* 33:278–285
- Bax L et al (2003) Influence of atherosclerosis on age-related changes in renal size and function: Atherosclerosis and renal size and function. *Eur J Clin Invest* 33:34–40
- Hoang K et al (2003) Determinants of glomerular hypofiltration in aging humans. *Kidney Int* 64:1417–1424
- Fuiano G et al (2001) Renal hemodynamic response to maximal vasodilating stimulus in healthy older subjects. *Kidney Int* 59:1052–1058
- van Londen M et al (2018) Renal functional reserve capacity before and after living kidney donation. *Am J Physiol Renal Physiol* 315:F1550–F1554
- Chen KW et al (2016) Compensatory hypertrophy after living donor nephrectomy. *Transplant Proc* 48:716–719
- Choi KH et al (2012) Clinical assessment of renal function stabilization after living donor nephrectomy. *Transplant Proc* 44:2906–2909
- Levey AS et al (2009) A new equation to estimate glomerular filtration rate. *Ann Intern Med* 150:604
- Lentine KL, Brennan DC, Schnitzler MA (2005) Incidence and predictors of myocardial infarction after kidney transplantation. *JASN* 16:496–506
- Froissart M, Rossert J, Jacquot C, Paillard M, Houillier P (2005) Predictive performance of the modification of diet in renal disease and Cockcroft-Gault equations for estimating renal function. *JASN* 16:763–773
- Chantler C, Garnett ES, Parsons V, Veall N (1969) Glomerular filtration rate measurement in man by the single injection methods using 51Cr-EDTA. *Clin Sci* 37:169–180
- Poggio ED et al (2006) Donor kidney volume and outcomes following live donor kidney transplantation: graft volume in living kidney donation. *Am J Transplant* 6:616–624
- Garg AX et al (2006) Proteinuria and reduced kidney function in living kidney donors: a systematic review, meta-analysis, and meta-regression. *Kidney Int* 70:1801–1810
- Kasiske BL et al (2013) A prospective controlled study of kidney donors: baseline and 6-month follow-up. *Am J Kidney Dis* 62:577–586
- Pabico RC, McKenna BA, Freeman RB (1975) Renal function before and after unilateral nephrectomy in renal donors. *Kidney Int* 8:166–175
- Ronco C, Bellomo R, Kellum J (2017) Understanding renal functional reserve. *Intensive Care Med* 43:917–920
- Gaillard F et al (2018) The age-calibrated measured glomerular filtration rate improves living kidney donation selection process. *Kidney Int* 94:616–624
- Lam NN et al (2020) Changes in kidney function follow living donor nephrectomy. *Kidney Int* 98:176–186
- Spinelli A et al (2017) Rationale for the evaluation of renal functional reserve in living kidney donors and recipients: a pilot study. *Nephron* 135:268–276

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.