## RESEARCH



# The utility of split function testing in determining recovery of glomerular filtration rate after living kidney donation: a cohort study

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## Abstract

**Background** A number of UK transplantation centres use isotope studies to estimate the relative contribution from each kidney in living kidney donor assessment. The evidence that the estimation of pre-donation split function of the non-donated kidney influences post-donation renal recovery is limited. The aim of this study was to analyse whether, in the context of other donor factors, the split function of the non-donated kidney predicts the percentage recovery of glomerular filtration rate (GFR) at one-year post-donation.

**Methodology** A retrospective cohort analysis was undertaken on 291 living kidney donors in the Glasgow Renal and Transplant Unit between 1<sup>st</sup> January 2011 and 1<sup>st</sup> June 2022. Univariable and multivariable linear regression analysis was used to analyse the impact of donor factors on recovery of renal function at one year relative to baseline isotope GFR (iGFR) or to estimated GFR (eGFR by Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] formula). Sub-analyses of donor outcome (% recovery of iGFR and eGFR at one year) were undertaken using single-measures ANOVA and grouping of donors by pre-donation isotope uptake of the non-donated kidney.

**Results** Median recovery of pre-donation GFR at 1 year was 70.0% (IQR 64.8-75.5). On linear regression analysis there was no significant association found between split function of the non-donated kidney and the percentage recovery of iGFR, although a small significant association was found for eGFR. There was no significant difference between mean iGFR or eGFR recovery on sub-analysis of donor outcomes.

**Conclusions** This study demonstrated no clinically important predictive relationship between percentage recovery of renal function at 1 year after living kidney donation and pre-donation split function within the range accepted for donation in our centre.

Keywords Donor outcome, Living kidney donor, Split function

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## Background

The assessment of living kidney donors requires the safeguarding of individuals from unacceptable healthcare outcomes, whilst avoiding unnecessary testing which is costly and which may restrict the donor pool or delay transplantation. In the UK, the assessment of living kidney donors includes accurate measurement of glomerular filtration rate by clearance of isotope (iGFR). Just under half of UK centres also routinely estimate the contribution from each kidney using an isotope study (renogram



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or DMSA scan) to calculate percentage function (personal communication). The remainder of centres use the measurement of split kidney function only when abnormalities are found on structural imaging.

This split function estimate may influence decision making about which kidney should be donated, usually with the assumption that leaving the donor with the 'better' kidney will reduce the risk of clinically significant reduction in kidney function in the longer term. Previous studies have shown that the non-donated kidney demonstrates hyperfiltration early after kidney donation so that, within a few weeks of donation, GFR is approximately 70% of pre-donation GFR [1]. The mechanisms for this and its long-term consequences are unclear [2, 3].

The British Transplantation Society (BTS) guidelines recommend that differential kidney function should be measured where there is > 10% variation in kidney size or a significant renal anatomical abnormality [4]. Kidney Disease Improving Global Outcomes (KIDGO) guidelines concur with this, highlighting that differential kidney function testing should be considered if there is a discrepancy in kidney length of greater than 2 cm [5]. The quality of evidence underpinning these recommendations is low. Furthermore the evidence of the correlation between kidney size and split renal function and the correlation between pre-donation measurements and donor renal outcomes is conflicting [6–9]. The aim of this study was to analyse whether, in the context of other donor factors, the relative percentage function of the non-donated kidney predicts the percentage recovery of GFR at one year (%recovery  $GFR_{1v}$ ) after kidney donation.

#### Methods

A retrospective cohort analysis was conducted of all living kidney donors undergoing donor nephrectomy at the Glasgow Renal & Transplant Unit between 1st January 2011 and 1st June 2022 inclusive. The Glasgow Renal & Transplant Unit is one of two tertiary centres in Scotland providing kidney transplantation services. It serves a population of approximately 2.5 million and manages approximately 40 adult living donors per year [10, 11]. The assessment of potential living donors in our centre follows UK national guidelines [4]. Lifelong donor follow-up data is routinely collected for the UK Living Donor Registry, as mandated by the Human Tissue Authority under the European Union Organ Donation Directive (EUODD), and co-ordinated in our centre by Living Donor Transplant Co-ordinators. During the period covered by this study our centre did not have defined acceptance criteria based on the reported split function. Rather the split function would be taken in the context of overall kidney function, morphological appearance of the kidneys, other risk factors for the donor and other available options for the intended recipient.

Data from the time of kidney donation extracted from the electronic patient record included: age, sex, predonation blood pressure (BP), body mass index (BMI), pre-donation isotope glomerular filtration rate (iGFR) (both absolute and body surface area corrected measurements), differential uptake on renogram (split function), pre-donation and 1 year post-donation serum creatinine (closest measure to one year within a window of 60 days either side of the one year window), and laterality of the donated kidney.

For the purposes of this study, donor sex was used as a demographic variable and defined as the sex categorisation designated to the individual at birth based on their physiological and physical features. One-year serum creatinine values were compared to the nadir post-donation serum creatinine and if  $\geq$  20% the electronic record was manually reviewed to ensure sampling during an episode of acute kidney injury was avoided, with an appropriate value within 60 days of the one-year date selected if applicable.

Isotope GFR was measured by clearance of chromium 51-ethylenediamine tetraacetic acid (EDTA, 3 MBq) or technetium 99 m diethylenetriamine pentaacetic acid (DTPA, 10 MBq). The slope-intercept method was used with four blood samples taken between two and five hours post radiopharmaceutical administration (approximately 120, 150, 180 and 240 min) [12]. Differential isotope uptake was assessed using technetium-99 m mercaptoacetyl triglycine (MAG3, 100 MBq) imaging and an integral method of calculating divided function in the renal cortices.

Donors were excluded from analysis if they donated at another centre, even if their follow-up was undertaken in Glasgow. Donors with missing data because their predonation assessment or follow-up care was carried out in another nephrology centre, or who did not have a serum creatinine measure sufficiently close to 1 year post-donation (<or > 60 days), were also excluded from analysis.

#### Estimating one year donor GFR

Donor iGFR is not routinely measured post-donation therefore an alternative was required to determine the 1-year post-donation donor GFR. Donor GFR at 1 year post-donation (GFR<sub>1y</sub>) was estimated from the deduction that, assuming muscle mass is unchanged, the ratio of GFR at 1 year post-donation to iGFR pre-donation (iGFR<sub>PD</sub>) is equal to the ratio of reciprocal serum creatinine at 1 year (SCr<sub>1y</sub>) to reciprocal creatinine predonation (SCr<sub>PD</sub>) (Fig. 1). This approach is novel but its validity is based on the principle applied in routine  $GFR_{1y} / iGFR_{PD} = (1/SCr_{1y}) / (1/SCr_{PD})$   $Thus: GFR_{1y} = ((1/SCr_{1y})/(1/SCr_{PD})) X iGFR_{PD}$  where:  $GFR_{1y} = estimate of iGFR at 1 year$   $iGFR_{PD} = isotopically measured GFR pre-donation$   $SCr_{PD} = serum creatinine pre-donation$   $SCr_{1y} = serum creatinine 1 year post donation$ 

Fig. 1 Equation demonstrating derivation of donor GFR at 1 year post-donation

clinical care that estimates of changes in kidney function (e.g. CKD-EPI eGFR) are dominated by changes in reciprocal of serum creatinine concentration.

## **Primary analysis**

The primary analysis was a univariable and multivariable linear regression analysis of the impact of the following independent variables from the time of donation on the dependent variable %recovery  $GFR_{1y}$ : age, sex, BP, BMI, laterality of kidney donated, iGFR and predonation functional split of the non-donated kidney on renogram. Two multivariable models were included— one with iGFR corrected for body surface area and one with uncorrected iGFR. Analysis was repeated using conventional estimated GFR (eGFR), calculated by CKD-EPI for both the pre-donation and 1 year estimate of GFR instead of iGFR and GFR<sub>1y</sub>calculation respectively [13]. The normality of distribution for all three models was improved by log-transforming the dependent variable.

#### Sub-analyses

Sub-analyses of donor outcome (%recovery GFR<sub>1y</sub>) were undertaken using single measures ANOVA and grouping of donors by pre-donation differential isotope uptake of the non-donated kidney. To do this kidney donors were characterised into three groups as follows: the non-donated kidney had pre-donation isotope uptake  $\geq$  55%; the non-donated kidney had pre-donation isotope uptake  $\leq$  45%; the non-donated kidney had pre-donation isotope uptake 46–54%. These groups were chosen on the basis of reference ranges for 'normal renal function,' and an international consensus that a difference in function of 10% or greater would be considered significant [5].

All statistical analysis was performed using Microsoft Office Excel 2013, and a *P*-value of < 0.05 was considered significant in primary and sub-analyses. The study design, with use of routinely collected patient data for the purposes of evaluating service performance for quality improvement, was classified as local service evaluation as opposed to research, therefore there was no requirement for review by the institutional research ethics committee. Approval for the analysis was obtained from the institutional data protection and information governance department.

## Results

There were 291 living kidney donors included in the analysis (Fig. 2) and donor characteristics are summarised in Table 1. Median age at donation was 49.9 (IQR [interquartile range] 40.4–56.7) years and 45.7% of donors were female (133). The majority of donors donated a left kidney (195, 67%).

## **Pre-donation renal function**

The median iGFR pre-donation was 89.9 (IQR 84–97) ml/min/1.73m<sup>2</sup>. Median eGFR pre-donation was 103.1 (IQR 94–110.3) ml/min/1.73m<sup>2</sup>.

Fifty-two donors had a non-donated kidney with  $\geq$  55% uptake with a range of 55–69%. Thirteen donors had a non-donated kidney with  $\leq$  45% uptake with a range of 42%-45%. The remaining 226 donated a kidney with isotope uptake between 46–54%.

### **Primary analysis**

The median  $GFR_{1y}$  was 62.8 (IQR 57.0–70.1) mL/ min/1.73m<sup>2</sup> and the median %recovery  $GFR_{1y}$  was 70.0% (IQR 64.8–75.5). Univariable and multivariable analyses were similar regardless if iGFR absolute or corrected



Fig. 2 Flow chart of study participant exclusions

for body surface area were utilised in calculations. In univariable analyses, donor age was inversely associated with %recovery GFR<sub>1y</sub> and donors of male sex had a significantly lower %recovery GFR<sub>1y</sub> compared with females (Table 2). Females recovered mean 73.6% of iGFR compared with male donors at 68.1% (P<0.005). Donor age and sex remained significantly associated with the %recovery GFR<sub>1y</sub> in multivariable analysis.

There was no significant association between %recovery  $GFR_{1y}$  and the laterality of kidney donated, predonation systolic or diastolic BP, pre-donation iGFR measurement and pre-donation BMI. There was no significant association between %recovery  $GFR_{1y}$  and the pre-donation isotope uptake of the non-donated kidney as determined by renogram (Table 2).

Table 1	Summary	of characteristics	of living	donors
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Number	291		
Median age (years)	49.9 (IQR 40.4-56.7)		
Female sex (no,%)	133 (45.7)		
Median pre-donation BMI (kg/m <sup>2</sup> )	27.2 (IQR 24.7-30.1)		
Median pre-donation systolic BP (mmHg)	130 (IQR 120–139)		
Median pre-donation diastolic BP (mmHg)	79 (IQR 72–84)		
Median pre-donation iGFR corrected for BSA (ml/min/1.73m <sup>2</sup> )	89.9 (IQR 84–97)		
Median pre-donation iGFR not corrected for BSA (ml/min)	102 (IQR 91.3–113)		
Median pre-donation eGFR (ml/min/1.73m <sup>2</sup> )	103.1 (IQR 94–110.3)		
Mean isotope uptake of non-donated kidney (%)	50.1 (SD 3.7)		
Mean difference in split function (%)	5.8 (SD 5.1)		
Left kidney donated (no, %)	195 (67)		
Median post-donation GFR at one-year corrected for BSA (ml/min/1.73m <sup>2</sup> )	62.8 (IQR 57.0-70.1)		
Median post-donation GFR at one-year not corrected for BSA (ml/min)	69.8 (IQR 62.2-80.7)		
Median one-year post-donation eGFR (ml/min/1.73m <sup>2</sup> )	70.4 (IQR 61.1-80.2)		

BP Blood pressure, BMI Body mass index, GFR Glomerular filtration rate, BSA Body surface area, eGFR estimated glomerular filtration rate

These analyses were repeated using eGFR calculated by CKD-EPI formula based on pre-donation and 1 year serum creatinine. Donor sex was significantly associated with %recovery of eGFR at one year (%recovery  $eGFR_1$ ) in both univariable and multivariable analyses. An association with pre-donation iGFR measurement, and an inverse association with increasing age and diastolic BP, with %recovery eGFR<sub>1v</sub> was noted in univariable analysis but not multivariable analysis. In multivariable analysis there was a significant association between decreased pre-donation isotope uptake of the non-donated kidney and reduced %recovery eGFR<sub>1v</sub> that was not found on univariable analysis (P < 0.05). Pre-donation systolic BP and laterality of kidney donated were not significantly associated with %recovery eGFR<sub>1v</sub> in univariable or multivariable analyses (Table 3).

#### Sub-analyses

There was no significant difference in %recovery iGFR<sub>1y</sub> between the pre-donation differential isotope uptake subgroups—non-donated kidney  $\geq$  55%, non-donated kidney  $\leq$  45%, non-donated kidney 46–54% (*P*=0.69) (Fig. 3). These analyses were repeated using eGFR calculated by CKD-EPI formula based on pre-donation and 1 year serum creatinine and there was again no significant difference in %recovery eGFR<sub>1y</sub> between the three groups (*P*=0.81). The median change in estimated iGFR and eGFR were not significantly different between each sub-group (*P*=0.50, *P*=0.64).

## Discussion

This study found no significant relationship between pre-donation differential isotope uptake of the nondonated kidney and the percentage recovery of the calculated iGFR one-year post-donation utilising the iGFR measurements prior to donation and reciprocal of serum creatinine before and at one year post donation. There was a significant association between pre-donation differential isotope uptake of the non-donated kidney and %recovery of kidney function at one year on multivariable linear regression analysis, and between pre-donation measured corrected iGFR and %recovery of kidney function at one year on univariable linear regression analysis when using %recovery  $eGFR_{1v}$  at one year as the outcome measure. Despite this, there was no significant difference in mean post-donation %recovery  $GFR_{1y}$  or %recovery eGFR<sub>1v</sub> regardless of whether the non-donated kidney was the better or lesser functioning kidney on renography. Additionally the median absolute change in  $GFR_{1y}$ and eGFR<sub>1v</sub> was not significant between the sub-groups of donors categorised by pre-donation isotope uptake of the non-donated kidney. The clinical value of pre-donation isotope split function measurement in predicting post-donation renal function at one year is therefore not clearly demonstrated by our study.

Our observation that living donors achieve approximately 70% of pre-donation GFR is consistent with previous studies [1, 2]. These studies have shown that the majority of this recovery takes place within a few weeks of donation. Little is known about the physiological mechanisms that regulate this response so consistently.

	Univariable l	inear regress	noi		Multivariable corrected for	linear regre body surface	ssion with iGF e area	ĸ	Multivariable corrected for	linear regree body surface	ssion with iGl e area	FR not
Variable	Co-efficient	Lower 95%	Upper 95%	<i>P</i> -value	Co-efficient	Lower 95%	Upper 95%	<i>P</i> -value	Co-efficient	Lower 95%	Upper 95%	P-value
Age	-0.0008	-0.0014	-0.0003	0.0019*	-0.0010	-0.0016	-0.0003	0.0028*	-0.0008	-0.0014	-0.0001	0.0176*
Male sex	-0.0304	-0.0418	-0.0190	< 0.0001*	-0.0280	-0.0398	-0.0161	< 0.0001*	-0.0299	-0.0447	-0.0151	0.0001*
Systolic BP	-0.0002	-0.0007	0.0002	0.2937	0.0004	-0.0002	0.0009	0.1800	0.0004	-0.0002	0.0010	0.1674
Diastolic BP	-0.0006	-0.0012	0.0001	0.0760	-0.0003	-0.0011	0.0004	0.3865	-0.0004	-0.0012	0.0004	0.3498
BMI	-0.0007	-0.0022	0.0008	0.3510	-0.0005	-0.0019	0.0010	0.5237	-0.0005	-0.0022	0.0012	0.5715
Right kidney donated	-0.0003	-0.0129	0.0124	0.9647	-0.0045	-0.0173	0.0084	0.4939	-0.0047	-0.0180	0.0087	0.4927
Corrected iGFR (ml/min/1.73m <sup>2</sup> )	-0.0001	-0.0006	0.0004	0.7594	-0.0004	-0.0010	0.0002	0.2245				
Uncorrected iGFR (ml/min/1.73m <sup>2</sup> )	-0.0003	-0.0006	0.0001	0.1178					< 0.0001	-0.0005	0.0005	0.9844
% isotope uptake of non-donated kidney	0.0012	-0.0004	0.0029	0.1318	0.0009	-0.0008	0.0026	0.2872	0.0009	-0.0008	0.0026	0.2961
BP Blood pressure, BMI Body mass index, i	'GFR isotope glom	erular filtration	rate									

Table 2 Summary of univariable and multivariable linear regression analysis of log-transformed % recovery of GFR at one year using pre-donation isotope glomerular filtration rate (iGFR) either corrected for body surface area or uncorrected for body surface area

Ē a) ' Blood pressur 

 Table 3
 Summary of univariable and multivariable linear regression analysis of log-transformed % recovery of estimated GFR (eGFR) at one year

	Univariable li	near regression			Multivariable linear regression			
Variable	Co-efficient	Lower 95%	Upper 95%	P-value	Co-efficient	Lower 95%	Upper 95%	P-value
Age	-0.0010	-0.0017	-0.0004	0.0009*	-0.0006	-0.0014	0.0001	0.1006
Male sex	-0.0236	-0.0373	-0.0099	0.0008*	-0.0247	-0.0386	-0.0107	0.0006*
Systolic BP	-0.0002	-0.0007	0.0003	0.5119	0.0005	-0.0001	0.0011	0.1065
Diastolic BP	-0.0009	-0.0016	-0.0001	0.0274*	-0.0007	-0.0016	0.0002	0.1528
BMI	-0.0011	-0.0028	0.0006	0.2218	-0.0007	-0.0023	0.0010	0.4269
Right kidney donated	-0.0078	-0.0226	0.0070	0.2991	-0.0133	-0.0285	0.0018	0.0845
iGFR (ml/min/1.73m <sup>2</sup> )	0.0008	0.0002	0.0014	0.0095*	0.0007	< 0.0001	0.0014	0.0562
% isotope uptake of non-donated kidney	0.0017	-0.0002	0.0036	0.0764	0.0023	0.0003	0.0042	0.0226*

BP Blood pressure, BMI Body mass index, iGFR isotope glomerular filtration rate



Fig. 3 Plot demonstrating non-significant differences in percentage recovery of pre-donation glomerular filtration rate (GFR) at 1-year between donor differential isotope uptake sub-groups

Our study adds to this in that, in apparently non-diseased kidneys, the relative contribution to GFR of the nondonated kidney before donation does not seem to play a significant part in determining this percentage recovery of pre-donation GFR at least within the range deemed acceptable for donation in our centre. Our study confirms the previously published observation that older age is associated with lesser compensatory increases in the function of the non-donated kidney [14– 16]. The fact that this was statistically significant in the analyses of % recovery of GFR based on iGFR but not the multivariable analysis of % recovery of eGFR might relate to age being included in the calculation of eGFR. Additionally our study is consistent with others in demonstrating lesser recovery of renal function post-donation in male compared with female donors [15]. The magnitude of the difference between males and females was small and probably of no clinical relevance. Van Londen et al., (2022) developed and validated a predictive equation for estimating 3 month post-donation iGFR which included donor pre-donation serum creatinine, age and sex, and this outperformed the use of pre-donation eGFR alone [17]. In our study, lower pre-donation diastolic blood pressure was associated with higher %recovery eGFR<sub>1v</sub> on univariable analysis although no association with %recovery iGFR<sub>1v</sub>. The presence of pre-donation hypertension has previously been noted to be negatively associated with ability of the non-donated kidney to undergo hyperfiltration [18].

Our study did not demonstrate a relationship between pre-donation BMI and recovery of either iGFR or eGFR post donation. A recent meta-analysis examining risks for living kidney donation noted a BMI of over 30 kg/m<sup>2</sup>to lower significantly the eGFR 1 year after donation [15]. Our donor population may not have included enough donors with BMI > 30 to detect this relationship (n=76). Our analysis did not find a significant association between laterality of kidney donated and donor renal recovery.

Our observations are useful for clinicians and potential donors when considering long-term kidney function and provide useful reassurance when a surgeon is considering donation of a kidney that has the lesser isotope uptake within the range observed in our study. The number of donors with split function of  $\leq 45\%$  in the non-donated kidney was small, but the absence of a clinically significant difference in outcome between these donors and those with a higher pre-donation split function is reassuring.

Previous studies have analysed other methods of assessing differential kidney function. Habbous et al., (2019) performed a meta-analysis to determine if computed tomography (CT) assessed split renal volume could predict split renal function as well nuclear renography [8]. In this meta-analysis, nine studies including 773 living donors reported on the ability of pre-donation split renal function to predict post-donation renal function (calculated through various formulae) between 2006 and 2017. The pooled correlation with eGFR was moderate with r=0.73 (95% confidence interval=-0.69-0.76). However, unlike our study, the majority of the included studies performed split function testing on selected living donors due to other concerns.

Eum et al., (2022) recently undertook a large study comparing CT volumetry and nuclear renography for predicting kidney function after living kidney donation in 835 donors [9]. They found split kidney function of the non-donated kidney on renography was significantly correlated with post donation kidney function at 1 month, 6 months and > 1 year although less predictive than CT volumetry in multivariable linear regression analysis. Donors were not routinely followed up beyond 6-months and therefore > 1 year post-donation function measurements were not available for the whole cohort.

Other recent smaller studies using differing methodologies to our own to examine the utility of split function in determining living donor and recipient outcomes have not found a consistent correlation with post-donation renal function. Seo et al., (2020) conducted a single-centre retrospective cohort analysis of the predictability of difference in pre-donation split renal function on eGFR at 6 and 12-month post-donation in 106 Korean living kidney donors [19]. Donors were split into three tertiles depending on the difference in pre-donation split renal function. The difference in split function was not associated with eGFR in any tertile at either 6 or 12 months.

In another recent retrospective cohort study of 248 Canadian living kidney donors up to 31 months post donation, renography was found to have no predictive value in estimating donor outcomes, including the subgroup of patients with a difference in split function that would be considered clinically significant [7]. This study compared predicted eGFR post-donation modelled on renography results (pre-donation eGFR x % split function of non-donated kidney) and observed eGFR post-donation. These results were compared with the predictive value of CT imaging estimations of split function on post-donation renal outcomes which also showed no significant correlation with observed eGFR [7].

Strengths of our study included the large cohort and that all donors in the programme had both a renogram and a direct pre-donation GFR measurement undertaken, thus minimising selection bias. Previous studies examining the predictability of split function on donor renal outcomes utilised eGFR measurement only [7, 9, 19]. The estimate of GFR at 1 year in our primary analysis utilising the iGFR pre-donation and the serum creatinine at 1 year is novel but based on the same physiological principle on which changes in eGFR are predicated (i.e. the relative changes are proportional to inverse of serum creatinine assuming there has been no change in muscle mass). To demonstrate this principle we plotted eGFR at 1 year post donation by CKD-EPI formula against estimated eGFR at 1 year derived from CKD-EPI eGFR pre donation and reciprocal of pre-donation and post-donation serum concentrations in the same way as shown in Fig. 1 for iGFR. This is shown in appendix 1 and demonstrates very close correlation. The method of estimating change in 1 year

GFR from the pre-donation iGFR and serum creatinine pre and post donation is likely to be more accurate than change in CKD-EPI eGFR because the baseline GFR was isotopically determined. Van Londen et al., (2022) determined that a predictive model using pre-donation isotope GFR and age to estimate post-donation iGFR outperformed both a model using creatinine, age and sex and a model using eGFR alone [17]. The gold standard would be a study utilising iGFR determined at one year as well as pre-donation but this has not been done to our knowledge.

This study had limitations that should be acknowledged. It is a single-centre retrospective cohort. However we utilised prospectively collected data in consecutive cases with no selection bias and we feel the results are likely to be generalisable to other centres where donors are selected according to published international guidelines. We used 1 year recovery of renal function as a surrogate for long-term kidney function outcome. This seems reasonable although one study showed evidence of continuing recovery of eGFR or measured iGFR up to 10 years [14, 17]. Some donors did not have a 1-year serum creatinine to enable inclusion but this was mainly due to geographical location rather than loss to follow-up and is unlikely to introduce a systematic bias. It is important to recognise that the results are limited to donors within the observed ranges of pre-donation iGFR and split function. It seems likely that the conclusions would be different if centres included donors with much lower iGFR or a much greater difference in split function as these hypothetical cohorts would likely include donors with significant kidney disease. Similarly, the conclusions cannot be extrapolated to potential kidney donors with evidence of other functional or structural renal abnormalities of kidneys excluded by standard donor assessment guidelines. There is an inherent bias in the sub-group analysis of donors split by differential isotope uptake given the likely confounding factors which were factored into the laterality of donation decision and the absence of a control group for comparison given that potential donors excluded from donating on the basis of split function were not considered. Other factors which have been demonstrated in other studies to have an influence on eGFR recovery or might be postulated to have an influence such as ethnicity, relationship of donor to recipient, smoking and history of treated hypertension were not included in our analysis [14].

## Conclusion

This study demonstrated no clinically significant nor consistently predictive relationship between %recovery of GFR at 1 year after living kidney donation and the relative pre-donation isotope uptake of the non-donated kidney within the range accepted for donation in our centre. This calls in to question whether routine split function measurement provides useful information in all living donors or should be limited to potential donors with low iGFR or a difference in kidney size on imaging.

## Appendix



Fig. 4 Plot demonstrating the correlation between CKD-EPI eGFR 1-year post donation measurement and estimated CKD-EPI eGFR 1-year post donation utilising reciprocals of pre and post donation serum creatinine

#### Abbreviations

BMI	Body mass index
BP	Blood pressure
BTS	British Transplantation Society
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CT	Computed tomography
DTPA	Diethylenetriamine pentaacetic acid
EDTA	Ethylenediamine tetraacetic acid
eGFR	Estimated glomerular filtration rate
GFR	Glomerular filtration rate
GFR <sub>1v</sub>	Glomerular filtration rate at 1 year
EUODD	European Union Organ Donation Directive
igfr	Isotope glomerular filtration rate
iGFR <sub>PD</sub>	Isotope glomerular filtration rate pre-donation
IQR	Interquartile range
KIDGO	Kidney Disease Improving Global Outcomes
MAG3	Mercaptoacetyl triglycine
SCr	Serum creatinine
SCr <sub>1v</sub>	Serum creatinine at 1 year
SCr <sub>PD</sub>	Serum creatinine pre-donation

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Not applicable.

#### Authors' contributions

Authors KC, CG, SM, AN and IM contributed to the conception and design of the study, and JG and KS contributed to the analysis and interpretation of the data. KC created the original drafts of the manuscript and all other authors contributed to manuscript revision. All authors approved the submitted version and agree to be accountable for all aspects of the work.

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#### Data availability

The data that support the findings of this study are available from NHS Greater Glasgow & Clyde but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from author CG (colin.geddes@ggc.scot.nhs. uk) upon reasonable request and with permission of NHS Greater Glasgow & Clyde.

## Declarations

#### Ethics approval and consent to participate

Approval for the analysis and consent to utilise anonymised data was obtained from the NHS Greater Glasgow & Clyde institutional data protection and information governance department (Caldicott). As per UK Health Research Authority guidelines, and decision tool accessible via their website (https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/) this service evaluation is not considered research and thus ethical approval is not required. This is because:

1. No interventions are being carried out in patients—this is an observation of clinical practice.

2. Data is collected after patient's usual care procedures from the procedures that they routinely undergo.

3. Only anonymised data is collected and uploaded onto a secure database. Informed consent from individual patients for this evaluation is not required as data is anonymised as per UK Health Research Authority and Scottish Executive Health Department guidelines.

#### **Consent for publication**

Not applicable.

#### **Competing interests**

CG is a council member of the UK Kidney Association and co-chair of the UK living kidney transplant network. KC, KS, JG, AN, IM and SM have no potential conflicts of interest to disclose.

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