

# Risks for donors associated with living kidney donation: meta-analysis

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## Abstract

**Background:** Living kidney donation risk is likely to differ according to donor's demographics. We aimed to analyse the effects of age, sex, body mass index (BMI) and ethnicity.

**Methods:** A systematic review and meta-analysis was undertaken of the effects of preoperative patient characteristics on donor kidney function outcomes, surgical complications, and hypertension.

**Results:** 5129 studies were identified, of which 31 met the inclusion criteria, mainly from the USA and Europe. The estimated glomerular filtration rate (eGFR) in donors aged over 60 years was a mean of 9.54 ml per min per 1.73 m<sup>2</sup> lower than that of younger donors ( $P < 0.001$ ). Female donors had higher relative short- and long-term survival. BMI of over 30 kg/m<sup>2</sup> was found to significantly lower the donor's eGFR 1 year after donation: the eGFR of obese donors was lower than that of non-obese patients by a mean of  $-2.70$  (95 per cent c.i.  $-3.24$  to  $-2.15$ ) ml per min per 1.73 m<sup>2</sup> ( $P < 0.001$ ). Obesity was also associated with higher blood pressure both before and 1 year after donation, and a higher level of proteinuria, but had no impact on operative complications. In the long term, African donors were more likely to develop end-stage renal disease than Caucasians.

**Conclusion:** Obesity and male sex were associated with inferior outcomes. Older donors (aged over 60 years) have a larger eGFR decline than younger donors, and African donors have a higher incidence of ESRD than Caucasians.

## Introduction

The waiting list mortality rate among kidney transplant candidates with end-stage renal disease (ESRD) ranges between 5 and 15 per cent<sup>1</sup>, with organ scarcity being the main determining factor.

Living kidney donation (LKD) represents the optimal treatment for kidney failure<sup>2,3</sup>. LKD significantly expands the organ pool, reducing waiting times and allowing a planned pre-emptive transplantation, thus ideally providing the best outcome in terms of patient and graft survival<sup>4,5</sup>.

Living donors are healthy individuals who voluntarily undergo risks related to their generous act, namely the surgical risks as well as potential longer-term consequences of nephrectomy. The assessment of these risks constitutes the basis for appropriate living donor selection, as the future health of the donor remains paramount.

The aim of this study was to systematically review the risk factors for living kidney donors in relation to short- and long-term outcomes.

## Methods

The study was registered with PROSPERO (CRD42020207052) before commencement of the literature search. The review was conducted and reported according to PRISMA guidelines<sup>6</sup>.

## Search strategy

Literature searches were performed in Ovid (Embase, MEDLINE), Web of Science, and Cochrane databases, using combinations of free text and keyword terms for living kidney donation and donor demographics of interest. A full search strategy is shown in *Appendix S1*. Searches were conducted on 14 November 2020.

## Inclusion and exclusion criteria

Any study relating donor risk factors to donor outcomes in living kidney donors was eligible for inclusion, including full articles and meeting abstracts. Only studies in English were included for analysis.

## Outcomes of interest

The primary objective was to assess the effect of donor demographics (ethnicity, BMI, age, and sex) on kidney function evaluated using estimated glomerular filtration rate (eGFR) adjusted for body surface area. Pretransplantation eGFR was compared with that 1 year after donor nephrectomy.

Secondary objectives included assessing the effect of donor demographics on incidence of ESRD, serum creatinine level at 1 year, donor survival, incidence of proteinuria, BP, *de novo* hypertension, and surgical complications.

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## Screening and data extraction

Study identification and data extraction was performed in three stages. The first stage included downloading the studies identified by the search strategy from Cochrane, Ovid, and Web of Science databases into EndNote™ (Thomson Reuters, Canada) reference management software. This software was then used to remove duplicate studies. The second stage included two independent researchers screening the titles and abstracts of longlisted studies. Each researcher produced a list of studies eligible for the review. The two lists were compared to produce a single shortlist of studies selected for full-text review. The third stage of data extraction comprised full reading of the shortlisted studies to identify those meeting the inclusion criteria. Data extraction was performed by two independent reviewers and disagreements were solved by discussion or by consulting another co-author. Data were extracted into a Microsoft® Excel spreadsheet (Microsoft, Redmond, Washington, WA, USA).

## Risk-of-bias assessment

Risk-of-bias assessment was undertaken using the National Heart, Lung, and Blood Institute quality assessment tool<sup>7</sup> (Appendix S2). Two independent reviewers judged the quality of the articles and compared their results. Risk-of-bias assessment was not carried out for four congress abstracts included in the study.

## Statistical analysis

All data analyses were performed in RevMan 5.4.1 (The Cochrane Collaboration, London) and SPSS® version 26 (IBM, Armonk, NY, USA). Meta-analysis of mean difference (MD) was used for continuous data. Random-effect models were used for all meta-analyses owing to the heterogeneous and small study samples. MDs with 95 per cent confidence intervals were calculated for the summary effect. The Z test was used to calculate P values. Where the 95 per cent confidence interval did not include 0, with  $P < 0.050$ , a statistically significant difference between the two groups was recorded. Forest plots were created in RevMan 5.4.1. Heterogeneity of the data was assessed using the  $I^2$  test; where the  $I^2$  value was greater than 0.5, the heterogeneity of the data was assumed to be high; otherwise, it was assumed to be low.

When it was necessary to combine two reported subgroups into a single group for meta-analysis (for example combining subgroup of donors aged 18–24 years with those aged 24–50 years into a single group for comparison with a group of donors aged over 50 years), the formula for combining groups from the Cochrane handbook<sup>3</sup> was used.

## Results

The literature search identified 5129 potentially eligible studies. Title and abstract screening identified 648 studies for full-text review, and eventually 31 studies met the inclusion criteria (Fig. 1). Fourteen studies were from Europe, 16 from the USA, and one was from China.

## Donor ethnicity

Seven studies reported on donor ethnicity. Three studies<sup>9–11</sup> compared eGFR before and after donation among different ethnicities, and followed patients for 1 year after nephrectomy. At baseline, African donors had a higher eGFR than their

Caucasian counterparts (MD 9.53 (95 per cent c.i. 0.77 to 18.28) ml per min per 1.73 m<sup>2</sup>;  $P=0.03$ ;  $I^2=76$  per cent) (Fig. S1a). However, 1 year after kidney donation, the eGFR of African donors was similar to that of Caucasian donors (MD 7.89 (–4.64 to 20.42) ml per min per 1.73 m<sup>2</sup>;  $P=0.22$ ;  $I^2=87$  per cent) (Fig. S1b).

Five studies<sup>12,16</sup> investigated the effects of donor ethnicity and incidence of ESRD in living donors. All studies used the Organ Procurement and Transplant Network (OPTN) database; therefore, overlap between the studies cannot be excluded and meta-analysis was not deemed appropriate. Three studies<sup>12,15</sup> reported a higher incidence of ESRD in African compared with Caucasian donors (Table 1). Lentine and colleagues<sup>13</sup> reported an increased incidence of chronic kidney disease (CKD) 7 years after donation in African donors (12.6 per cent of 611) compared with Caucasian donors (5.6 per cent of 3458). The same study demonstrated a higher incidence of donor proteinuria in African compared with Caucasian donors. However, these results are different from those reported by Jain et al.<sup>17</sup> who found no significant differences between African and Caucasian donors in terms of proteinuria and eGFR at 1 year (Table 2), but lengths of follow-up were different.

## Donor BMI

### Effect of donor BMI on kidney function

Three studies<sup>11,18,19</sup> examined the effects of donor BMI on eGFR corrected for body surface area 1 year after donation; the first two also reported donor eGFR values before donation (Fig. S2a). One year after LKD, the eGFR in donors with a BMI above 30 kg/m<sup>2</sup> was a mean of 2.70 (95 per cent c.i. –3.24 to –2.15) ml per min per 1.73 m<sup>2</sup> lower than that of donors with a BMI under 30 kg/m<sup>2</sup> ( $P<0.001$ ). The heterogeneity in the analysis was low ( $I^2=12$  per cent) (Fig. S2b).

### Effect of obesity on BP in kidney donors

Two studies<sup>18,20</sup> recorded the BP of kidney donors before donation and at 1-year follow-up.

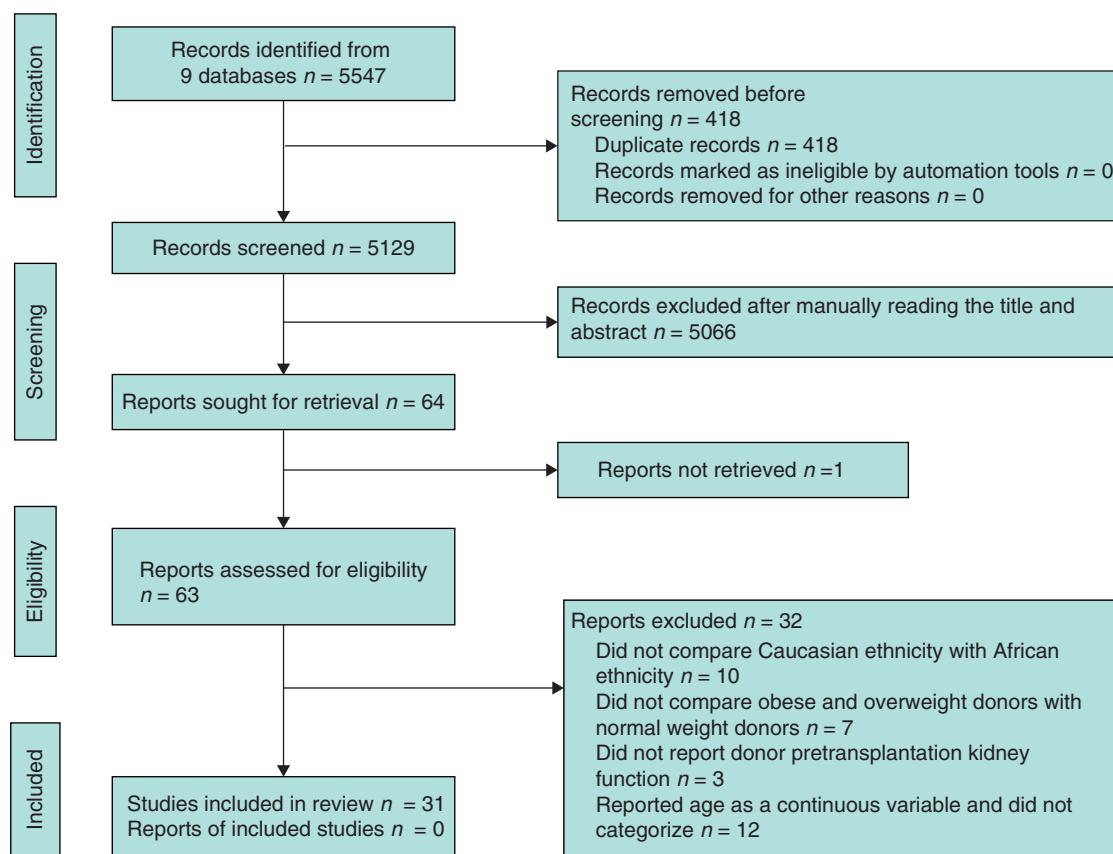
These studies presented contradictory evidence on the predonation systolic BP of kidney donors; in one<sup>20</sup> it was significantly higher among obese compared with non-obese donors (MD 12.5 (95 per cent c.i. 12.93 to 12.1) mmHg;  $P<0.001$ ), whereas no significant difference was observed in the other study<sup>18</sup>, (MD –2.10 (CI: –4.46 to 0.26) mmHg;  $P=0.22$ ). Both studies reported a significantly lower systolic BP in non-obese donors 1 year after kidney donation, and a significantly lower diastolic BP in non-obese donors before and after donation.

### Effect of BMI on development of proteinuria in donors

Four studies<sup>21–24</sup> with different follow-up times examined the effects of donor BMI on the development of proteinuria after LKD (Table 3).

Two studies<sup>21,24</sup> compared the median or mean amount of urinary protein at the end of the study period. The first study<sup>21</sup> compared donors with BMI less than versus over 25 kg/m<sup>2</sup>, and found no significant difference related to proteinuria ( $P=0.28$ ). The other<sup>24</sup> noted that the level of proteinuria was significantly higher in donors with a BMI over 30 kg/m<sup>2</sup> than in donors with a BMI below 30 kg/m<sup>2</sup> ( $P=0.027$ ).

Two studies<sup>22,23</sup> reported numbers of patients with protein in the urine above a certain defined threshold (Table 3). Both



**Fig. 1** PRISMA flow chart showing selection of articles for review

studies found the prevalence of proteinuria to be statistically significantly higher in obese donors after LKD; however, the findings of one study<sup>22</sup> demonstrated a clinically non-significant difference between non-obese and obese donors at the end of follow-up (5.3 versus 6.3 per cent prevalence of proteinuria). The other study<sup>23</sup> reported a clinically significant finding as 92 per cent of obese renal donors developed proteinuria during the study interval compared with only 12 per cent of non-obese donors.

### Effect of BMI on development of postoperative complications in donors

Four studies<sup>22,25–27</sup> recorded no statistically significant difference in the occurrence of surgical complications according to donor BMI.

### Donor age

#### Effect of donor age on kidney function assessed by eGFR

Three<sup>12,18,28</sup> studies reported the effects of donor age on LKD after eGFR. Before LKD, donors aged less than 60 years had a significantly higher eGFR than those older than 60 years (MD 5.28 ml per min per 1.73 m<sup>2</sup>;  $P < 0.001$ ;  $I^2 = 0$  per cent) (Fig. S3a). One year after LKD, the difference in eGFR between donors aged less than 60 years and older donors had increased further (MD 9.54 (95 per cent c.i. 6.91 to 12.16) ml per min per 1.73 m<sup>2</sup>;  $P < 0.001$ ;  $I^2 = 45$  per cent) (Fig. S3b), possibly in relation to a differing compensatory capacity between the two groups.

#### Effect of age on donor kidney function assessed by serum creatinine level

Four studies<sup>18,28,30</sup> investigating effect of age on serum creatinine concentration met the inclusion criteria. The first two<sup>18,28</sup> compared serum creatinine levels before and 1 year after LKD in donors who were younger or older than 60 years. The remaining two studies<sup>29,30</sup> compared serum creatinine levels before and 1 year after LKD in individuals aged less than versus more than 50 years.

Before LKD, there was no significant difference between serum creatinine levels between donors older than 60 years and those aged less than 60 years ( $P = 0.11$ )<sup>18,28</sup>, although, as expected, levels in younger donors were on average lower numerically (MD  $-0.97$  (95 per cent c.i.  $-2.16$  to  $0.22$ )  $\mu\text{mol/l}$ ). One year after LKD, the difference in serum creatinine levels between donors older or younger than 60 years became significant ( $P = 0.006$ )<sup>18,28</sup>. The serum creatinine levels of younger donors were a mean of  $4.37$  ( $-7.49$  to  $-1.26$ )  $\mu\text{mol/l}$  lower than those of older donors.

Before LKD, donors younger than 50 years had a slightly lower serum creatinine concentration than donors older than 50 years (MD  $2.80$  ( $-4.24$  to  $-1.36$ )  $\mu\text{mol/l}$ ;  $P < 0.001$ ). One year after LKD, there was no significant difference in serum creatinine levels between donors older or younger than 50 years (MD  $-12.5$  ( $-31.31$  to  $6.32$ )  $\mu\text{mol/l}$ ;  $P = 0.19$ )<sup>29,30</sup>.

#### Effect of age on survival of donors

Four studies<sup>28,31–33</sup> analysed survival rates according to age at donation, demonstrating no significant difference between the

Table 1 Donor ethnicity in relation to end-stage renal disease after living kidney donation

Reference	Source of data	Population characteristics	ESRD data reported as	ESRD incidence				Significance of difference in incidence of ESRD between races
				Caucasian donors	African donors	Asian donors	Hispanic donors	
Muzaale et al. <sup>12</sup>	OPTN (donors) and NHANES (control group of non-donors). CMS database to see which donors developed ESRD	Cohort of 96 217 who donated a kidney between April 1994 and November 2011 in the USA. Matched non-donor population derived from NHANES III survey carried out between 1988 and 2004. Participants censored at death	Cumulative incidence of ESRD at 15 years after donation. Per 10 000 patients undergoing unilateral nephrectomy for kidney donation	22.7 (15.6, 30.1) per 10 000 (n=71 778)	74.7 (47.8, 105.8) per 10 000 (n=12 412)		32.6 (17.9, 59.1) per 10 000 (n=12 027)	Groups were not compared inter-racially; comparison made between ESRD incidence in donors and healthy non-donors
Lentine et al. <sup>13</sup>	OPTN database and an unspecified database from a national private health insurer	Individuals with records of serving as a live kidney donor in the USA between October 1987 and July 2007 and benefits under the participating insurer after donor nephrectomy at some point in May 2000 to December 2007. Total of 4069 living related donors selected	Incidence of CKD 7 years after donation compared between donors of African and Caucasian ethnicities. Groups stratified for donor age and sex	n=3458; 5.6% of Caucasian donors developed CKD	n=611; 12.6% of African American donors developed CKD			Adjusted HR for African American versus Caucasian donors 2.32 (1.48, 3.62) (P < 0.001)
Gibney et al. <sup>14</sup>	OPTN/UNOS database	UNOS/OPTN searched for all patients awaiting a kidney transplant between 1993 and 2005 who were previously kidney donors. These data were compared with frequencies of donors of various races, who donated a kidney between 1993 and 2005	Numbers of patients from each ethnicity awaiting a kidney transplant between 1993 and 2005. Percentage of living donors by race who donated between 1993 and 2005 compared with percentage of living donors of that race listed for transplant between 1993 and 2005	41 donors awaiting a transplant; 42 419 patients donated a kidney	45 donors awaiting a transplant; 8889 patients donated a kidney	2 donors awaiting a transplant; 1879 patients donated a kidney	2 donors awaiting a transplant; 7375 patients donated a kidney	Caucasian donors had a significantly lower proportion of living donors listed for transplant (40%) compared with number of living donors (68%) (P < 0.001). African American donors had a significantly higher proportion of living donors listed for transplant (44%) compared with number of living donors (14%) (P < 0.001). Results for other races not significant
Wainright et al. <sup>15</sup>	OPTN database and CMS database	Development of ESRD in people who donated a kidney between 1994 and 2016 in the USA. Donors were censored by death and end of study period	Development of ESRD determined as the earliest record of either beginning maintenance dialysis, being put on a transplant wait list or undergoing transplantation	113 of 86 501 donors developed ESRD	70 of 15 219 donors developed ESRD		24 of 15 914 donors developed ESRD	Adjusted HR for African versus Caucasian donor ESRD incidence 2.79 (1.92, 4.06) (P < 0.001). Adjusted HR for Hispanic versus Caucasian donor ESRD incidence 1.29 (0.80, 2.07) (P = 0.29)
Wainright et al. <sup>15</sup>	OPTN and CMS databases	Development of ESRD among first-degree related living donors who donated a kidney between 1994 and 2018	Not stated in this abstract	115 of 45 700 donors developed ESRD	83 of 10 214 donors developed ESRD			P value not presented in abstract (P < 0.001, $\chi^2$ test, calculated by review authors)

Values in parentheses are 95 per cent confidence intervals. ESRD, end-stage renal disease; OPTN, Organ Procurement and Transplant Network; NHANES, National Health and Nutrition Examination Survey; CMS, Centers for Medicare & Medicaid Services; CKD, chronic kidney disease; UNOS, United Network for Organ Sharing; HR, hazard ratio.

older and younger donor age groups in the short to medium term. In particular, Segev and colleagues<sup>33</sup> compared mortality every 2 years after kidney donation between donor age groups and an

aged-matched group of non-donors for 12 years. The conclusion was that mortality rate was not significantly increased after a median of 6.3 years.

**Table 2 Donor ethnicity in relation to incidence of proteinuria after living kidney donation**

Reference	Study type	Donor population characteristics	Proteinuria incidence		Significance of difference between incidence of proteinuria between races
			Caucasian donors	African American donors	
Lentine et al. <sup>13</sup>	Cohort study	Total of 4069 living related donors followed for 7 years after LKD	90 of 3458 (2.6%)	35 of 611 (5.7%)	By 7 years after donation, proteinuria was more common in African than Caucasian donors: adjusted HR 2.27 (95 per cent c.i. 1.32, 3.89) ( $P < 0.050$ )
Jain et al. <sup>17</sup>	Cohort study	522 living kidney donors followed for 1 year after LKD	3 of 43 after 1 year	7 of 73 after 1 year	Compared with Caucasians, African American and Hispanic donors did not have an increased risk of developing hypertension, proteinuria, or decreased eGFR up to 12 months after LKD

LKD, living kidney donation; HR, hazard ratio; eGFR, estimated glomerular filtration rate.

**Table 3 Effect of BMI on incidence of proteinuria in donors after kidney donation**

Reference	Study characteristics	Duration of follow-up	Outcome measured	BMI groups of donors (kg/m <sup>2</sup> )					Significance of difference between higher BMI and lower BMI groups	
				< 18.5	> 18.5, < 25	> 25, < 30	> 30, < 35	> 35	Before donation	After donation
van Londen et al. <sup>22</sup>	105 female living kidney donors; 54 had BMI < 25 kg/m <sup>2</sup> , 51 had BMI > 25 kg/m <sup>2</sup>	Proteinuria measured 2 months after surgery	Median (range) protein excreted in urine in g per 24 h	BMI < 25 kg/m <sup>2</sup> (n = 54): 0.0 (0.0–0.2) g per 24 h before LKD; 0.0 (0.0–0.2) g per 24 h after LKD		BMI > 25 kg/m <sup>2</sup> (n = 51): 0.0 (0.0–0.2) g per 24 h before LKD; 0.0 (0.0–0.2) g per 24 h after LKD g/24 h			P = 0.72 (Student's t test)	P = 0.28 (Student's t test)
Serrano et al. <sup>23</sup>	3752 donors; 3096 had BMI < 30 kg/m <sup>2</sup> , 656 had BMI > 30 kg/m <sup>2</sup>	Donors followed for 20 years after LKD	Prevalence of proteinuria in renal donors 20 years after LKD. Proteinuria defined as excretion of > 150 mg/day	BMI < 30 kg/m <sup>2</sup> : prevalence of proteinuria 165 of 3096 (5.3%) after 20 years		BMI > 30 kg/m <sup>2</sup> : prevalence of proteinuria 41 of 656 (6.3%) after 20 years			–	Unadjusted P < 0.001 (Fisher's exact test); adjusted P = 0.21 (logistic regression adjusted for donation year and surgery type)
Praga et al. <sup>24</sup>	73 donors; 59 had BMI < 30 kg/m <sup>2</sup> , 14 had BMI > 30 kg/m <sup>2</sup>	Donors followed up for mean(s.d.) 13.6(8.6) years after LKD	Proteinuria defined as > 0.0 g protein per day in urine	BMI < 30 kg/m <sup>2</sup> : prevalence of proteinuria 7 of 59 (12%) at follow-up		BMI > 30 kg/m <sup>2</sup> : prevalence of proteinuria 13 of 14 (92%) at follow-up			–	P < 0.001 ( $\chi^2$ test)
Tavakol et al. <sup>25</sup>	98 donors; 82 had BMI < 30 kg/m <sup>2</sup> , 16 had BMI > 30 kg/m <sup>2</sup>	Kidney donors followed up 5–40 years after LKD	Mean(s.d.) 24-h urine protein excretion measured in mg per day before and after LKD	BMI < 30 kg/m <sup>2</sup> : 68(45) mg/day before LKD; 113(52) mg/day after LKD		BMI > 30 kg/m <sup>2</sup> : 80(30) mg/day before LKD; 146(62) mg/day after LKD			P = 0.407 (t test)	P = 0.027 (t test)

LKD, living kidney donation.

### Effect of age on development of proteinuria in donors

With regard to the incidence of proteinuria after LKD in relation to age at donation, Moutzouris et al.<sup>34</sup> found no significant difference between donors younger than 60 years versus those aged over 60 years (mean(s.d.) 0.12(0.06) versus 0.12(0.01) g per 24 h respectively;  $P = 0.87$ ). Dols and colleagues<sup>31</sup> reported no statistical differences in the incidence of proteinuria at 1, 5, and 10 years after donation between donors younger or older than 60 years.

### Effect of age on development of complications in donors

Kostakis et al.<sup>35</sup> found no significant difference in the incidence of intraoperative or postoperative complications between donors

younger or older than 60 years ( $P = 0.78$ ). Both Dols and colleagues<sup>31</sup> and Gero et al.<sup>28</sup> divided the complications experienced by donors into minor and major complications, according to the Clavien–Dindo classification<sup>36</sup>, but only Gero and co-workers found that younger donors had a significantly lower rate of minor postsurgical complications ( $P < 0.001$ ); outcomes were comparable for major ones (Clavien–Dindo grades III–IV) ( $P = 0.363$ ).

### Donor sex

#### Effect of donor sex on BP

Four studies<sup>37–40</sup> investigated the effect of donor sex on the incidence of hypertension post-LKD (Table 4). Rook and colleagues<sup>37</sup> and Najarian et al.<sup>38</sup> compared donor BP before

Table 4 Effect of donor sex on BP

Reference	Outcome measured	Study participants	Follow-up	BP (mmHg)*		Significance (M versus F)
				M	F	
Rook et al. <sup>38</sup>	Systolic/diastolic BP	125 donors; 45 M, 80 F	56 days after kidney donation	Before LKD (n = 45): 125(11)/76(8) After LKD (n = 45): 130(13)/80(7)	Before LKD (n = 80): 122(11)/74(8) After LKD (n = 80): 125(14)/78(8)	Systolic P = 0.146 Diastolic P = 0.182 Diastolic P = 0.163 (Student's t test)
Najarian et al. <sup>39</sup>	Systolic/diastolic BP	63 donors; 27 M, 36 F	20 years after LKD	Before LKD (n = 27): 124(3)/79(2) After LKD (n = 27): 130(4)/77(2)	Before LKD (n = 36): 115(2)/74(2) After LKD (n = 36): 137(3)/81(1)	Systolic P < 0.001 Diastolic P < 0.001 Systolic P < 0.001 Diastolic P < 0.001
Tent et al. <sup>40</sup>	Mean arterial pressure	293 donors; 131 F, 162 M	2 months after LKD	Before LKD (n = 131): 95(9) After LKD (n = 131): 96(9)	Before LKD (n = 162): 91(9) After LKD (n = 162): 92(9)	P < 0.001  P < 0.001
Holscher et al. <sup>41</sup>	Incidence of postdonation hypertension requiring medical treatment	37 901 donors; 14 232 M, 23 669 F	2 years after LKD	440 of 14 232	483 of 23 669	P < 0.001 ( $\chi^2$ test)

Values are mean(s.d.). LKD, living kidney donation.

and after LKD, and reported no significant difference, in case of Rook et al, or significant, in case of Najarian et al.<sup>38</sup>, between men and women at either time point. Furthermore, Tent et al.<sup>39</sup> observed men to have a significantly higher mean arterial pressure than women, but with no significant differences before and after LKD. In a large study, Holscher and co-workers<sup>37</sup> investigated the incidence of hypertension in donors 2 years after LKD, and reported a higher proportion of men than women with hypertension.

### Effect of donor sex on renal function in donors

Three studies<sup>12,28,41</sup> investigated the effect of sex on the variation in eGFR before and after LKD. (Fig. S4). There was no significant difference in eGFR between men and women, either before LKD (MD 4.14 (95 per cent c.i. -3.55 to 11.85) ml per min per 1.73 m<sup>2</sup>; P = 0.29; I<sup>2</sup> = 88 per cent) or 1 year after donation (MD (-4.99 to 8.52) ml per min per 1.73 m<sup>2</sup>; P = 0.61; I<sup>2</sup> = 91 per cent).

Concerning the effect of sex on the development of ESRD, the analysis included three studies<sup>13,16,42</sup>, all deriving from the OPTN/United Network for Organ Sharing (UNOS) databases and reporting a significantly higher incidence of ESRD in male donors after kidney donation compared with female donors (risk ratio 2.24<sup>42</sup>; risk ratio 1.95<sup>13</sup>; adjusted hazard ratio (HR) 1.75<sup>16</sup>).

### Effect of donor sex on survival

Two studies<sup>28,33</sup> reported on donor survival according to sex. Gero and colleagues<sup>28</sup> followed 213 donors, and reported no deaths among men and women in the first year after LKD. In a much larger study by Segev et al.<sup>33</sup>, which used the OPTN/UNOS database consisting of records of all donors who donated a kidney between 1994 and 2009 in the USA, mortality rates were low but differed significantly between the sexes at 1 year (0.1 per cent of male versus 0.03 per cent of female donors) and 12 years (2.7 versus 1.9 per cent respectively; HR 1.75, 95 per cent c.i. 1.5 to 2.0), with a risk ratio of 3; the authors did not comment on the reasons for the difference.

## Discussion

No significant difference was found in donor kidney function (assessed by eGFR) 1 year after LKD between African and

Caucasian donors. In the long term, African donors were more likely to develop ESRD than Caucasian donors. However, it is unknown whether the risk of developing ESRD is higher in kidney donors than in the general population, and the higher incidence of ESRD among African kidney donors could reflect the higher risk of development of ESRD for people of African ethnicity compared with Caucasians. The data on effect of race on development of proteinuria are heterogeneous, so it is not possible to conclude whether African ethnicity increases donor risk of developing proteinuria compared with Caucasian ethnicity. This present findings suggest that ethnicity *per se* is not a contraindication to donation, and that educational campaigns aimed at increasing awareness of the benefits of LKD, particularly for kidney transplant candidates who have waited for a long time<sup>4</sup>, should be considered carefully before discarding prospective living donors. In this regard, there is an ongoing debate regarding the use of ethnicity for prediction models of renal function, with the assumption that use of the chronic kidney disease epidemiology collaboration formula could have offered adjustments to estimates<sup>43</sup>. Yet, although it is true that ethnicity correlates with the frequency of particular genomic variants at population level, it cannot be used exclusively to predict a patient's response, as it could relate only to general socioeconomic status or educational level, and therefore not be causing an effect<sup>44</sup>.

Donor obesity (BMI over 30 kg/m<sup>2</sup>) was associated with a significantly lower donor eGFR 1 year after LKD. However, this finding may not be clinically significant as the eGFR of obese donors was only a mean of 2.70 (95 per cent c.i. -3.24 to -2.15) ml per min per 1.73 m<sup>2</sup> lower than that of non-obese patients. Donor obesity was associated with significantly higher systolic and diastolic BPs both before and 1 year after LKD, although it is not possible to conclude definitively that hypertension occurs at a higher rate among donors than in the general population<sup>45</sup>. Higher rates of proteinuria were associated with donor obesity, but donor BMI did not have an impact on the incidence of intraoperative and postoperative complications. It could be concluded, therefore, as in the case of kidney transplant candidates, that BMI of less than or greater than 30 kg/m<sup>2</sup> is not a reliable cut-off for identification of eligible living donors<sup>46</sup>.

The present study confirmed that donors aged over 60 years had a lower eGFR and higher serum creatinine levels before and after donation compared with younger donors<sup>28</sup>. Yet, this finding was not observed when a cut-off of 50 years was used; before LKD, donors aged less than 50 years had slightly lower serum creatinine levels than those aged 50 years or more (MD 2.80 (95 per cent c.i. -4.24 to -1.36)  $\mu\text{mol/l}$ ;  $P < 0.001$ ). However, 1 year after LKD, there was no significant difference between these two groups (MD -12.5 (-31.31 to 6.32)  $\mu\text{mol/l}$ ;  $P = 0.19$ ), so the kidney function of younger donors might have deteriorated. This highlights the need for strict lifelong follow-up, particularly for those who have a long life expectancy, as the risk of ESRD could increase when a lower eGFR after donation among younger donors is observed.

In terms of surgical risks, a single study<sup>28</sup> found a greater incidence of minor complications (Clavien–Dindo I–II) in donors older than 60 years compared with those aged less than 60 years, but not in the incidence of major postoperative complications (Clavien–Dindo III–IV).

As regards sex, male donors were found to have a significantly higher risk of developing ESRD after LKD than female donors, in accordance with reports highlighting a more severe course of kidney failure in men<sup>47,48</sup>. Furthermore, donor mortality was found to be slightly higher in men both in the short term (1-year survival rate 0.1 per cent versus 0.03 per cent in women) and long term (12-year survival rate 2.7 versus 1.9 per cent) after kidney donation.

The present meta-analysis has some limitations. First, the retrospective nature of the studies analysed has limited the level of evidence, based on observational registry data, small number of studies, and heterogeneity. None of the published studies in this meta-analysis reported individual-patient data. With regard to studies comparing obesity, different BMI categories were used, the main division being obese (BMI over 30  $\text{kg/m}^2$ ) and non-obese (BMI under 30  $\text{kg/m}^2$ ) donor groups. Fewer studies reported greater granularity of donor BMI, and the studies were not sufficient to create a meta-analysis with a higher level of granularity. For this reason, the formula for combining several groups outlined in the Cochrane handbook<sup>9</sup> was used to form two groups of non-obese and obese donors. Similarly, the studies used different age groupings; to gather enough data for the meta-analysis, donor groups from several studies had to be combined, which limited the granularity of the analysis significantly.

Disclosure. The authors declare no conflict of interest.

## Supplementary material

Supplementary material is available at *BJS* online.

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