Outcome of the living kidney donor

Pierre Delanaye¹, Laurent Weekers¹, Bernard E. Dubois¹, Etienne Cavalier², Olivier Detry³, Jean-Paul Squifflet³ and Jean-Marie Krzesinski¹

¹Department of Nephrology, Dialysis, Transplantation, University of Liège, CHU Sart Tilman, Liège, Belgium, ²Department of Clinical Chemistry, University of Liège, CHU Sart Tilman, Liège, Belgium and ³Department of Abdominal Surgery and Transplantation, University of Liège, CHU Sart Tilman, Liège, Belgium

Correspondence and offprint requests to: Pierre Delanaye; E-mail: pierre_delanaye@yahoo.fr

Abstract
Renal transplantation from living kidney donors is still relatively marginal in most of the European countries. However, this source of kidney grafts may help to overcome in part the organ donor shortage of cadaveric donors. The living donor strategy implies correct and objective information about donation risks and completely free acceptance of the living candidate of the donation. In this paper, we reviewed the consequences of kidney donation on the living donor health, considering very short term (linked to the surgery), short term (effect of nephrectomy on glomerular filtration rate) and long term (risk of mortality, chronic kidney disease, proteinuria and hypertension) consequences of kidney donation.

Keywords: glomerular filtration rate; hypertension; living kidney donor; proteinuria

Introduction

The first kidney transplantation (KT) was performed in 1954 from a living donor [1]. Due to limitations in immunologic knowledge, the first transplantations were actually performed between homozygote twins. With the progress in immunology and development of anti-rejection therapies, there was an increase in deceased donor transplantation. However, KT from living donors was continued because it brings with it several advantages. Advantages of the transplantation from living kidney donors compared to deceased donors are numerous but beyond the scope of this review [2].

The prevalence of KT from living donors varies widely throughout the world. For example, the proportion of KT from living kidney donors is 3.3% in Finland, 8% in France, 12% in Belgium, 21.6% in Germany, 47% in the UK [3], 49.5% in the USA [4], 63.8% in the Netherlands and 80% in Japan [5]. In some countries like Egypt and Pakistan, this kind of KT is the sole method of escaping from the dialysis treatment [6, 7].

In living KT, the priority should be not to harm the living kidney donors who must be carefully selected to limit the risks, especially the risk of developing chronic kidney disease (CKD). Living kidney donor criteria are beyond the scope of this review [8, 9]. Nevertheless, the first rule for living donation is, of course, having a normal glomerular filtration rate (GFR). However, GFR normality is not clearly defined, especially in elderly patients [9]. The range of normal GFR references varies according to the method used to measure (which must probably be recommended) or estimate GFR [8–10]. From a theoretical point of view, an optimal kidney donor should not suffer from arterial hypertension (HTA) or proteinuria. These living kidney donors are actually often
considered as healthy subjects [11]. *Sensu stricto*, this assertion must be tempered by the analysis of the American registry where living donors present obesity (20%), HTA (2%) and proteinuria (3.5%) [4]. This article reviews the potential risks of living kidney donation for the donor. More recent data on this topic have been published since the last review published in *Nephrology, Dialysis, Transplantation* by Gai et al. in 2007 [12].

**Reduction in renal mass**

The renal consequences of acute reduction of nephron mass, as after a nephrectomy, were already studied at the end of the 19th century [13]. Thirty years ago, Barry Brenner developed an elegant theory of the pathophysiological consequences of nephron mass reduction [14–16]. After nephrectomy, the remaining kidney presents a functional adaptation by an increase in renal filtration in every single nephron due to the increase in intraglomerular pressure [17–19]. This renal hyperfiltration is reflected by a quantifiable increase in renal plasma flow, which is accompanied by an increase in intraglomerular pressure [20, 21]. This renal hyperfiltration, and especially the increase in intraglomerular pressure, may eventually adversely impact the kidney function on the long term. Embolization with microspheres in renal arteries of rats can lead to ischaemia in 10% of glomeruli, without reduction in GFR. However, this ischaemic insult will favour glomerular capillary HTA and progressive sclerotic injuries in the remaining non-ischaemic glomeruli [22]. This phenomenon has been confirmed in rat experiments of 5/6 nephrectomy that leads progressively to end-stage renal disease (ESRD) [18, 19]. In this animal model, a hyperfiltrating glomerulus is firstly observed with a progressive increase in the glomerulus size. Thereafter, morphological lesions will appear, notably in the glomerular basement membrane, which will be reflected by proteinuria appearance [18, 23]. These lesions will continue to develop until fibrosis and the observation of the typical focal and segmental glomerulosclerosis [18, 23, 24]. Renal reduction mass seems also concomitant to the development of systemic HTA [16, 25].

However, it must be underlined that a nephronic reduction of 50% in a healthy subject is probably not entirely comparable to a 5/6 renal mass reduction in the rat [26, 27]. This will be illustrated by most of studies we are discussing in this review.

**Acute mortality and morbidity**

It is obvious that the post-operative mortality risk for living kidney donation is very limited. However, because death of a living donor is rightly considered as dramatic, some previous data should be reviewed. In 1973, post-operative mortality was estimated at 0.1% in USA [2]. In the 1980s, this percentage decreased to 0.04% [28] and at the end of the 20th century, it was even lower (0.01–0.03%). These American data have been obtained from registries with a very large sample [4, 29–32]. The most recent data calculated the mortality risk at 90 days (which is *sensu stricto* not equivalent to post-operative mortality) and it has been determined to be 0.031%. These data were calculated from a population of 80,347 kidney donors from 1994 to 2009 in USA (in this vast study, data from only 36 patients were lacking) [33]. This mortality risk is far lower than that observed in the USA (2.6%) in patients after a nephrectomy for causes other than donation [34] but, of course, the latter patients have a fully different profile of morbidities [33]. In kidney donors, the 90-day mortality is higher in men than in women (5.1 versus 1.7 per 10,000 donors), in Afro-Americans than in Caucasians (7.6 versus 2.6 per 10,000 donations) and in hypertensive patients than in normotensive people (36.7 versus 1.3 per 10,000 donors). However, the mortality was not influenced by age and remains stable during the 15-year study period even if the surgical techniques have moved from ‘open’ to laparoscopic methods [33]. In this large study, there was no data on the cause of death but pulmonary embolism probably remains a classical cause [5, 31]. Concerning the major morbidities linked to the procedure (myocardial infarction, spleen lesion, wound infection and bleeding), prevalence seems also relatively low and have been estimated at 1.8% in 1987 [28]. These first data were confirmed by other authors thereafter with prevalence from 1.6 to 3.8%, according to the definition retained for major complications [4, 5, 30, 35–43]. Since the 1990s, several authors have proposed laparoscopic procedures which allow kidney donation with lower post-surgical pain and shorter hospitalization duration [44–46]. The rate of complications, and notably the rate of hospitalization for ileus, is significantly higher for the laparoscopic technique even if the global rate of such complications may be considered low (1.2–1.6%) [30].

**Short-term consequences of donation on GFR**

The Table 1 summarizes the principal publications about the early modifications of the GFR level [48, 50–53, 55, 58, 60, 63]. We selected studies having used reference methods to measure GFR [10]. One of the first studies was published in 1958 by Bricker et al. after kidney donation between young homozygote twins. The authors showed that the donor inulin clearance decreased from 147 to 68 mL/min 1 month after donation but increased to 74 and 84 mL/min after 7 and 8 months, respectively [64]. Data published after this first article were even more optimistic. To summarize, it can be stated that, in the healthy young (<60 years old) donors, post-donation GFR reaches 65–70% of the pre-donation GFR [47, 49, 50].

The compensatory mechanism starts very early after nephrectomy. Some authors have actually shown an increase in GFR as soon as 8 h after the donation (with a measured GFR at 66% of the pre-donation GFR) [48]. This acute compensation is, however, less efficient in elderly subjects [52, 55, 59, 63, 65, 66] as it is related to the use of the renal functional reserve (measured by dopamine infusion). This ability to functional renal adaptation actually decrease by half after donation [58, 60, 67] or even more in old or obese patients [60, 62]. Recently, Barri et al. observed from a sample of 196 patients that post-donation GFR measured by a reference method (iothalamate clearance) could decrease under the threshold of 60 mL/min in 27% of the
### Table 1. Short-term evolution of GFR in living kidney donor

<table>
<thead>
<tr>
<th>Authors, publication date (reference)</th>
<th>Sample</th>
<th>Population and mean follow-up</th>
<th>Measured or estimated GFR</th>
<th>% GFR after/before or GFR after</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krohn, 1966 [47]</td>
<td>29</td>
<td>Homozygote donor 21–54 years 1–18 days</td>
<td>Creatinine clearance</td>
<td>71 ± 10%</td>
</tr>
<tr>
<td>Sugino, 1967 [48]</td>
<td>9</td>
<td>Homozygote donor 8 h 1 week 1 month 6–11 days</td>
<td>Inulin</td>
<td>66 ± 10% (66 ± 14%) 70 ± 13%</td>
</tr>
<tr>
<td>Donadio, 1967 [49]</td>
<td>4</td>
<td>21–45 years 116 ± 6 mL/min 1 week 4 weeks 3–6 months &gt;6 months</td>
<td>Diatrizoate</td>
<td>68–75%</td>
</tr>
<tr>
<td>Flanigan, 1968 [50]</td>
<td>24</td>
<td>21–63 years 111 ± 3 mL/min 1–3 weeks 3 months 6 months 1 year</td>
<td>Inulin</td>
<td>66%</td>
</tr>
<tr>
<td>Olander, 1968 [51]</td>
<td>13</td>
<td>Not precise 22 women 21–63 years 111 ± 3 mL/min</td>
<td>Inulin</td>
<td>+50%</td>
</tr>
<tr>
<td>Boner, 1973 [52]</td>
<td>49</td>
<td>20–65 years 110 ± 5 mL/min 10–14 days</td>
<td>Inulin or iothalamate</td>
<td></td>
</tr>
<tr>
<td>Davison, 1976 [54]</td>
<td>9</td>
<td>36–56 years 97 ± 9 mL/min 1 week 4 men 48–58 years 101 ± 14 mL/min 1 week</td>
<td>Creatinine clearance</td>
<td>70%</td>
</tr>
<tr>
<td>Aurell, 1981 [55]</td>
<td>15</td>
<td>24–64 years 1 day 4 days 7 days 1 year</td>
<td>Inulin at 12 months 55Cr-EDTA at 1, 4 and 7 days</td>
<td>66%</td>
</tr>
<tr>
<td>Bertolatus, 1985 [56]</td>
<td>22</td>
<td>19–61 years 116 ± 4 mL/min 1 week 1 month 6 months 1 year</td>
<td>Creatinine clearance</td>
<td>72 ± 4 mL/min 78 ± 4 mL/min 88 ± 5 mL/min 77 ± 6 mL/min</td>
</tr>
<tr>
<td>Mimran, 1993 [57]</td>
<td>18</td>
<td>20–62 years 47 ± 3 years 125 ± 8 mL/min 14 ± 1.4 months 42 ± 3 years 111 ± 6 mL/min 1.3 ± 0.3 months</td>
<td>Creatinine clearance</td>
<td>62%</td>
</tr>
<tr>
<td>Ter Wee, 1994 [58]</td>
<td>12</td>
<td>19 women 88 ± 12 mL/min/1.73m² 20–35 years 26 ± 3.9 45 women 113 ± 13 mL/min/1.73m² 1 week 6 months</td>
<td>Iothalamate</td>
<td>69 ± 4 mL/min</td>
</tr>
<tr>
<td>Velosa, 1995 [59]</td>
<td>32</td>
<td>51 years (61 ± 5.6) 19 women 88 ± 12 mL/min/1.73m² 20–35 years (26 ± 3.9) 45 women 113 ± 13 mL/min/1.73m² 1 week 6 months</td>
<td>Inulin or iothalamate</td>
<td>66 ± 10% (n = 88) 68 ± 8% (n = 65)</td>
</tr>
<tr>
<td>Rook, 2008 [60]</td>
<td>178</td>
<td>61% women 48 ± 11 years 114 ± 20 mL/min 2 months</td>
<td>Iothalamate</td>
<td>64 ± 7%</td>
</tr>
</tbody>
</table>

*Continued*
population, especially in older patients. This decrease in GFR is, however, not considered as deleterious by the authors because it occurs only in 10% of patients <30 years but in 91% for those aged from 60 to 69 years [63]. Moreover, GFR ~60 mL/min may be considered as normal in elderly healthy subjects because GFR physiologically decreases according to age [63, 68]. These authors also confirmed that GFR estimation from creatinine-based equations [Modification of Diet in Renal Disease (MDRD) or Cockcroft] is not accurate to estimate true GFR both before and after donation [11, 61, 63, 69–71]. This underlines the difficulties for GFR follow-up after nephrectomy. So, to be more accurate, it would be better to measure and not to estimate the GFR in this population [7, 61, 69, 71, 72].

**Long-term consequences of donation: a preliminary methodological discussion**

By nature, the issue of the long-term consequences of kidney donation for the donor is much more difficult to study. Indeed, if kidney donation was deleterious on the donor’s GFR or health status, this would be apparent only after a very long period (10 or even 20 years). Such long longitudinal studies are very difficult to perform. Actually, only a few academic centres will systematically follow their donors over the long term [73]. Therefore, very few longitudinal and prospective studies exist and almost all are monocentric [74, 75]. Our knowledge on this aspect is actually based on retrospective and transversal data.

There are also methodological limitations in such studies because definition of the followed parameters can vary with time, inducing discrepancies between the studies’ results. For example, the definition of HTA has changed from the 1960s to today. Methods for creatinine measurement have also changed with time (for example, the current enzymatic methods give systematically lower creatinine values than the prior Jaffe methods) which make the interpretation of creatinine slopes very difficult. This will be still more relevant if creatinine-based equations are retrospectively used. Contrary to the acute consequences on GFR, few studies exist on the long-term consequences of donation on GFR by reference methods [54, 74–77].

Another problem is the increasing number of patients lost to follow-up because it could be presumed that such patients are those with the worst outcome. The best follow-up observed in studies varies from 87 to 100% of the initial population [76, 78, 79] but in several studies, the percentage of patients actually followed is much lower.

When reviewing the available data concerning long-term risk for mortality, CKD or ESRD, proteinuria and/or HTA, these parameters are clearly influenced by age. Data observed in the donors must thus be analysed in comparison to a controlled group matched, at least, for age. The ideal study would be to follow a group of donors and controls matched for age and for risk factors associated with CKD progression. However, such a study does not exist and most often, data from epidemiological studies in the general population are used as the control group. However, this method may be misleading because the overall health status in living kidney donors could be considered better than in the general population, even if matched for age [80].

**Long-term consequences of donation**

**Mortality**

Strong and valid data about the long-term mortality of living kidney donors are not easy to find. Indeed, such studies are necessarily long and complex (with a large sample needed). One of the first studies regarding mortality was published by Mathillas et al. in 1988. These authors described 10 deaths of 64 donors followed for 5–15 years and this incidence was not considered as different from the general Swedish population [74]. The second study was published in 1997 by the same group and is still considered as one of the most important trials in the field. Mortality was calculated from a sample of 430 Swedish donors (which corresponds to >80% of the donors in this centre). The authors describe 41 deaths occurring from 15 months to 31 years after the donation. Once again, for these authors, this mortality rate is 30% less than the mortality observed in the general Swedish population [38]. In 2008, Garg et al. published the results observed in 1278 Canadian donors who were matched for age, gender and health status with 6369 controls. The follow-up of this study was relatively limited (6.4 years) but the mortality observed in the donors group (0.5%) was quite similar to the mortality observed in the control group (0.9%) [81]. The same conclusion can be drawn for the cardiovascular end points. In 2009,
a Japanese study was published including 481 donors (80% of the donors in this centre) and found a mortality rate after 5–30 years of follow-up which was the same as in a general population matched for age and gender [5]. Another recent study compared 12-year mortality observed in 39,516 American donors to a control group matched for age and health status (no HTA, no proteinuria) from the epidemiological NHANES study (n = 80,347). Mortality rate according to age was significantly less in the donor group (1.3% for donors <40 years, 3.5% for donors between 50 and 59 years and 9.4% for donors >60 years). However, among donors, African-American and hypertensive had a significantly higher mortality rate [33]. The most recent study was from Norway and was of interest because all kidney donors between 1963 and 2007 (n = 2,269) have been included (all KTIs are performed in one centre in Norway). The overall and cardiovascular mortality after a mean follow-up of 14.7 years was compared to the general population matched (3:1) for age (data from the Norwegian health system). In this study, overall (324 donors died) and cardiovascular mortality was lower in kidney donors. Only in the oldest donor group (70–79 years), was the mortality higher in the donor group, but the sample was relatively limited (n = 75) [78].

All these studies show that living kidney donors do not have a higher mortality risk compared to the general healthy population.

Risk of accelerating loss of GFR

This risk is not easy to comprehend. Indeed, GFR loss is physiologically observed after 40 years [2, 15, 82–84]. Therefore, the potential deleterious effect of kidney donation would be an accelerating decrease of the physiological GFR slope, which is not easy to demonstrate. First data date back to the 1960s and 1970s but both sample size and follow-up length are relatively limited. The first study results using a reference method for GFR measurement are summarized in Table 2. In 1973, Boner et al. showed the results of 19 donors followed for 2 or 3 years. The GFR was at 65% of the pre-donation GFR. In this study, the authors performed a multivariate analysis demonstrating that post-donation GFR would be dependent on pre-donation GFR, transplantation vintage and donor age [52]. Comparable results were also published in the 1970s using creatinine clearance [20, 85]. The most interesting study in the 1970s was certainly published by Slack and Wilson [84] from the Mayo Clinic in 1976. These authors measured GFR before and after donation in 121 donors. However, the time interval between the pre- and post-donation GFR measurement was still rather short and too heterogeneous (from 2 weeks to 6 years) which makes the interpretation of the results difficult. In this study, the post-donation GFR was measured at 60–70% of the pre-donation GFR [84].

All these results, obtained with reference methods for GFR measurement, could thus be considered as reassuring. However, in these trials, both the samples and the follow-up lengths were limited. In the following years, studies were published with larger samples and the length of follow-up increased. However, these studies were transversal and retrospective, and more importantly, the GFR was no longer measured but estimated either by creatinine-based equations or by creatinine clearance [69, 70]. Among the studies published in the 1980s [74, 86–95], the mean follow-up could reach from 15 to 20 years [74, 91, 92, 94, 95]. Once again, the vast majority of results are reassuring assuming that post-donation GFR is between 66 and 85% of the pre-donation GFR [86, 87, 89, 92, 93, 95]. Only two studies measured GFR by a reference method (but on a limited sample) and found comparable results [90, 93]. In the 1990s and at the beginning of the 21st century, the number of studies published on this topic has grown. Compared to prior studies, several recent studies have ultimately added little value [7, 43, 96–102]. We will thus concentrate on the most interesting data, notably on studies with the most important follow-up (≥20 years) and the best methodology [6, 31, 75–77, 79, 103–105]. In 2001, Goldfarb et al. measured the creatinine clearance in 70 donors (from a global population of 180) with a mean follow-up of 25 ± 3 years. In these patients, estimated GFR is still at 72% of the pre-donation GFR [103]. The study proposed by Saran et al. [75] is interesting for at least two reasons: the mean follow-up is long (19.5 ± 5 years) and the GFR has been measured by an isotopic method. Forty-one donors among 47 had a measured GFR which might be considered as normal according to their age (normal reference of GFR is compared to values given by another publication [106]). In the six remaining donors, measured GFR was only slightly decreased. A recent publication in the New England Journal of Medicine by Ibrahim et al. [77] is also of interest and has become a classical study on this topic. The authors have measured GFR by iohexol in 255 donors. The study is original because the authors have included donors according to their years of follow-up. Moreover, these donors are thought to be representative of the whole population of donors in this American centre between 1963 and 2007 (n = 3698). The mean follow-up was 12 ± 9 years. Eighty-five percent of donors had a measured GFR >60 mL/min which seems, once again, excellent. Comparable results have been published by Ferham-Elkhom and Grossman with cohorts where very few donors had been lost to follow-up [76, 79, 107]. We have to comment on the recent meta-analysis published by Garg et al. [105] in 2006. The authors have compiled data from 36 studies (n = 3529) where GFR was estimated (by any methods) with a mean follow-up of 6 years. In this meta-analysis, the estimated GFR was calculated at 86 mL/min which is relatively positive but the follow-up is limited. In eight studies with a follow-up of at least 10 years, Garg et al. showed that 40% of donors have an estimated GFR between 60 and 80 mL/min, 12% between 30 and 59 mL/min and 0.2% <30 mL/min.

### Table 2. Evolution at long-term (>12 months) of GFR after living kidney donation*

<table>
<thead>
<tr>
<th>Authors, date of publication (reference)</th>
<th>Sample</th>
<th>Mean follow-up</th>
<th>Method</th>
<th>GFR after/GFR before (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donadio, 1967 [49]</td>
<td>4</td>
<td>16 m</td>
<td>Iothalamate</td>
<td>81</td>
</tr>
<tr>
<td>Ogden, 1967 [66]</td>
<td>17</td>
<td>35 m</td>
<td>Inulin</td>
<td>71</td>
</tr>
<tr>
<td>Boner, 1973 [52]</td>
<td>19</td>
<td>2 to 3 y</td>
<td>Iothalamate</td>
<td>65</td>
</tr>
<tr>
<td>Slack, 1976 [84]</td>
<td>121</td>
<td>2 to 6 y</td>
<td>Inulin</td>
<td>60–70</td>
</tr>
</tbody>
</table>

*Studies from the 1970s with measured GFR. m, months; y, years.
min. Nevertheless, as the authors themselves underline, heterogeneity between the studies was very high, notably due to differences in the methodology. Recently, it was published, from a cross-sectional retrospective study on a population of 573 kidney donors (mean age at donation 47 years, nephrectomized between 1965 and 2005), that the GFR (measured by either Cr-EDTA clearance or ioethyl or estimated from the MDRD equation) with a follow-up of 14 years increased during the five years after donation and decreased thereafter [107]. Several authors have studied factors which could influence a more important decrease in GFR values. The most cited factor associated with the risk of decreased GFR is doubtless the age, which is not fully surprising [20, 66, 75, 88, 89, 93, 102]. Interestingly, high body mass index (BMI) has also been associated with the risk of a lower post-donation GFR in the study of Ibrahim et al. [77] which is probably one of the best studies from a methodological point of view. In a recent work restricted to donors with a private health insurance in the USA, it was suggested that the risk of Stage 3 CKD (GFR < 60 mL/min) was influenced by ethnicity as it was doubled in African-American and in Hispanic-American donors compared to Caucasian donors [108].

Risk of ESRD

The probability to develop ESRD after living donation is fortunately very low. However, this evolution is not impossible. The classical example is the subject with a kidney familial disease, such as atypical haemolytic syndrome, who has given a kidney to a relative and developed the disease after. However, it seems that diabetes and congestive heart failure are among the most frequent causes of ESRD in donors [40, 77, 94, 104]. In the study by Ibrahim [77], 11 donors have progressed to ESRD. Risk of developing ESRD is thus estimated at 180 cases/million/year. This incidence of ESRD must be compared to the incidence observed in the general population (not matched for health status) which is much higher, at 268 cases/million/year. From the Swedish study between 1965 and 2005, 6 donors of 1112 have progressed to ESRD (incidence rate of 0.5%) [109]. ESRD was reached from between 14 and 27 years after the donation (and the donors were then between 45 and 89 years old). This incidence rate is lower than the one observed in the general population but the difference becomes non-significant if the general population is matched for age. Another method to estimate the incidence of donors reaching ESRD is to examine prior donors from the waiting list for KT in the USA [110–112]. With this methodology, the results are less optimistic. Moreover, these results must be analysed keeping in mind that some prior donors could not be enrolled on the list for medical reasons. In 2008, Gibney et al. [111] described 104 donors (i.e., 0.16%) on the waiting list for KT from a group of 62,327 living donors in the USA between 1996 and 2006. More importantly, among these donors on the waiting list, African-Americans are over-represented (40%) although they represent only 14% of the whole living kidney donor population [111, 112]. This higher risk of ESRD in African-American living donors seems to be confirmed in recent data from American registries [108]. Moreover, it must be underlined that such African-American donors are frequently under-represented in clinical trials on the topic (for example in the studies of Ibrahim and Fehrman-Ekholm [76, 77]).

Risk of proteinuria

The risk of proteinuria is quite real and described in most of the studies but fortunately, this complication occurs only in a minority of donors. The proteinuria will be <1 g/24 h in the vast majority of donors. More severe and nephrotic proteinuria are exceptional [75, 79, 86–89, 93, 104, 113], even in studies with the largest follow-up [103, 104]. Regarding proteinuria, drawing one unique conclusion is very difficult because results from all these studies are very heterogeneous. The percentage of proteinuric patients may actually vary from 0 to 34% according to studies (notably because the definition of proteinuria may also vary). In the Fehrman-Ekholm (proteinuria screening with dipstick) and Ibrahim (albuminuria measurement) studies, proteinuria prevalence was 9 and 12%, respectively [76, 77]. Few studies with limited samples have compared the risk of proteinuria between donors and a control group like related subjects [31, 95] or healthy subjects [74, 89, 93, 102]. A higher prevalence of proteinuria is found in most (but not all [31]) of these studies [74, 89, 93, 95, 102]. The meta-analysis proposed by Garg et al. [105] also stresses the results' heterogeneity and the absence of a control group in most of the studies. This author compiled the results of 42 trials (n = 4793) with a mean follow-up of 7 years (which is relatively short). The prevalence is then calculated at 12%. According to this meta-analysis, the risk for developing proteinuria is higher than in the general population. However, it remains very difficult to precisely quantify this risk and to determine the factors favouring its development. More importantly, up to now, there is no strong scientific proof of a systematic continuum between proteinuria development and CKD progression in the living kidney donor. Additional studies on the prevalence of proteinuria and, especially, on its potential role as a 'renal' prognostic marker in the kidney donors seem necessary.

Risk of HTA

Risk of de novo HTA must also be discussed. As for other risks, there are concerns with the HTA definition and measurement. Moreover, the lack of control group is, once again, a limitation observed in many studies. Several studies have shown that donors significantly increase their systolic and/or diastolic arterial pressure after kidney donation [79, 89, 90, 93, 114]. In most of these studies, this increase in arterial pressure is statistically significant but clinically limited and most of the donors do not reach values to be considered as hypertensive. We will discuss the studies with a sufficient sample and a control group because it is well known that prevalence of HTA also increases with ageing in the general population. In 1984, Weiland et al. [94] followed 472 American donors for 8 ± 5 years and described a prevalence of HTA of 6.7% which was then considered as identical to the prevalence observed in the general population. The same conclusion is reached by authors from different countries [6, 79, 86]. Fehrman-Ekholm [76] found that 38% of HTA
was not considered as different from the prevalence in the Swedish general population (results being analysed according to age). Very recently, according to a retrospective study from the same group, HTA prevalence was re-evaluated at 43% of patients from a population of 573 kidney donors [107]. Donors followed by Goldfarb et al. for a mean of 25 years were 64 years old. In this study, HTA prevalence reached 48%. This prevalence is, however, lower than the prevalence in the NHANES study for subjects aged from 65 to 74 years old (54%) [103]. On the contrary, other studies found a higher prevalence of HTA in the donors compared to the general population, especially after 50 years [75, 87, 113]. In 2006, Boudville et al. [114] published a meta-analysis on the topic. Once again, the authors insisted on the great heterogeneity in the results and the frequent absence of a control group in the 48 studies analysed. However, the authors described an increase of 5 mmHg in the 5–10 years following the kidney donation [114]. Recent data have yet suggested that non-Caucasian donors could have a higher risk of HTA [108].

Risks associated with donor’s obesity

One striking observation from the American registry is that 19.5% of subjects are selected for donation although they are obese [4]. These data must be interpreted in the context of physiological data showing that obese patients have glomerular hyperfiltration [115], epidemiological data showing that obesity is a strong risk factor for ESRD [116] and clinical data showing that obesity is a risk factor for proteinuria and CKD after nephrectomy in urological diseases [117]. Data having specifically studied the outcomes of obese donors are relatively few but very recent [7, 77, 113, 118, 119]. These authors have suggested that obesity was associated with a higher risk of de novo HTA in donors. However, a control group is lacking in all these studies and it is well known that obesity is also associated with a higher risk of HTA in the general population. Only one study has included a control group in their analysis but the sample was relatively limited (81 donors and only 16 obese). The control group was selected and matched to age, gender, ethnicity and BMI from the NHANES study. In this study, there is not a significantly higher risk of HTA for the obese donors compared to obese in the general population. Estimated GFR was also comparable in the two groups but it must be underlined that the estimation of GFR is especially difficult in the obese population [72]. The risk of proteinuria is, however, higher in obese donors [119]. Ibrahim et al. [77] have shown that body surface area was a risk factor for measured GFR <60 mL/min/1.73m². For some authors, the more frequent obesity in African-American subjects could, at least in part, explain the over-representation of the African-American donors on the waiting list for transplantation [111]. Additional studies seem necessary.

Other risks related to donation

Another concern recently raised by some authors is the potential higher risk for complications in pregnancy (gestational HTA or diabetes, pre-eclampsia, fetal loss) after kidney donation. Two recent studies have illustrated this topic [120, 121]. Both studies showed that there is no additional risk for gestational complications after kidney donation compared to the non-matched general population. However, the risk of eclampsia could be higher if the comparison is done in the same women donors before and after kidney donation [120, 121].

Psychological consequences of kidney donation must not be forgotten, as well as the socio-economic consequences [4, 122, 123]. If kidney donation is realized in good conditions, these potentially harmful consequences will be avoided (no familial or financial stress, free consent after complete and loyal information, pre-donation psychological evaluation) [124, 125]. The vast majority of donors (95–99%) do not regret donation, especially when donation is a success for the related subjects [5, 44, 122, 126]. Several studies (including a multicentre one [41]) demonstrated a correct quality of life in donors in the long term [41, 122, 126–128]. Some American data from registries are, however, less optimistic as it was noted that the rate of suicide was higher in donors than in the general population (14 per 100 000 versus 10.96 per 100 000) [4].

Conclusions

Harmful outcomes for the living kidney donors seem limited. The living kidney donation may be considered as safe. This safety is, however, dependent on the selection criteria retained for kidney donation. In this view, the percentage of obese or proteinuric subjects eventually selected for kidney donation in the USA is somewhat questionable. Harmonization for the follow-up of the donors should also be welcome. From our point of view, the living kidney donors should be followed for HTA, proteinuria and GFR. In this view, we think that donors should benefit from repeated measured GFR for better assessment of the GFR slope. Additional studies, notably in specific donors (obese, African-American), are still needed to better comprehend the outcomes of these subjects who have given a part of their healthy body to a diseased human.

Conflict of interest statement. None declared.

References

a cross-sectional retrospective study. *Nephrol Dial Transplant* 2011; 26: 2377–2381


Received for publication: 8.8.11; Accepted in revised form: 20.10.11