

Long-Term Donor Outcomes After Living Kidney Donation

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Abstract

Kidney transplant is the first choice of treatment for end-stage renal failure. The issue of long-term donor safety again has been raised by recent increases in living-donor kidney transplants worldwide, relaxation of donor selection criteria, and the introduction of new surgical techniques.

In this review, we collated the results of various studies to discuss the effects of donation on the quality of life of donors, encompassing their physical, mental, and social well-being. We found that the health risks donors face are minimal in the long term with respect to renal function, hypertension, and life span. Furthermore, donors scored higher in quality of life studies than did persons in the general population. Despite these findings, there is a clear need to monitor the minimal risks with long-term follow-up of donors to promptly recognize and treat any negative health effects. Such data from thorough follow-up studies also would provide accurate information on long-term donor health and improve the safe expansion of donor selection criteria.

Key words: *Transplant, Renal, Quality of life*

The first successful kidney transplant from a living donor was done in the United States in 1954 by Joseph Murray in Boston, Massachusetts. Today, living-donor kidney transplant is the well-established treatment of choice for the ever-

increasing number of patients with end-stage renal failure offering longer survival and a better quality of life at a lower cost than dialysis (1-4). Living donors include genetically related donors (eg, parents, offspring, and siblings) and unrelated donors (eg, spouses, partners, friends, and altruistic strangers) (5).

The number of living donors has been increasing worldwide, and the World Health Organization estimated that in 2005, of the 66 000 total kidney transplants in the world, 25 500 were from living donors (6). Rates vary worldwide, but the highest percentages of kidney transplants from living donors come from South East Asia and the Middle East. In India, more than 95% of kidney transplants are from live donors (1, 2, 6). These rates most probably reflect the lack of resources and infrastructure to organize a program of deceased-donor donation and procurement (6-8). However, in developed countries, the number of transplants from live donors is increasing too, and in 2001, the annual number of kidney transplants from living donors in the United States surpassed that from deceased donors (2). Similarly, in the United Kingdom, the British Transplant Society reported in 2005, that there has been significant growth in living-donor kidney transplants over the previous 5 years (9). The substantial increase in the numbers of kidney transplants from live donors in developed countries reflects the constantly decreasing numbers of deceased donors as well as the improved surgical techniques for live-donor nephrectomy, in addition to patient awareness and increased recognition of the merits of living donation (1, 6, 7, 10). These benefits include the avoidance of long wait times on dialysis, better transplant planning, and superior (to deceased-donor kidney transplant) recipient and allograft survival rates (1, 8, 10, 11). Furthermore, live-donor kidney transplant can be performed

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preemptively (before initiating dialysis), with better outcomes compared with live-donor kidney transplants done after the initiation of dialysis (1, 2, 12).

The Hippocratic principle states “first do no harm” and dominates the ethical code of medical practice around the world. It applies even more so for live kidney donors: healthy individuals who have nothing to gain for their own health and who only benefit from an altruistic feeling of improving the health of another human being (7, 10, 13, 14).

The rapid increase in the number of live-donor kidney transplant programs around the world has, as expected, intensified the interest of patients, health care professionals, and the larger community regarding the short- and long-term risks to the donor (7, 8). Hence, many studies have aimed at evaluating risks to the donors, and these studies have focused not only on long-term kidney function (as was the case in the past) but on a wide range of physiological, psychological, and quality of life factors (15).

Long-term effect of donation on physical health (Table 1)

Creatinine clearance and glomerular filtration rate

A follow-up study by Schostak and associates found that after a median postoperative period of 7 years, the mean serum creatinine level was 89.9 $\mu\text{mol/L}$ in female and 114.2 $\mu\text{mol/L}$ in male donors (16). A meta-analysis found an average serum creatinine level of 98 $\mu\text{mol/L}$ from 36 studies at a mean of 6 years after donation, while the predonation mean from all 48 studies was 81 $\mu\text{mol/L}$ (17). Although studies show an increase in creatinine levels after donation, levels stay within the normal range in most patients; 1 study found only 1.5% of donors had creatinine levels above 153 $\mu\text{mol/L}$ after a mean follow-up of 10.7 years (8).

Creatinine values can vary with differing sizes of patients, and so glomerular filtration rate (GFR) is a more-accurate estimate of renal function (17). A follow-up study by Gossman and associates found the mean GFR had fallen significantly from 92 to 71 mL/min/1.73 m² ($P < .001$) at an average of 11 years after donation (15). Another study found a mean GFR of 64 mL/min/1.73 m² in donors at an average of 12 years after donation. The GFR values for each individual were compared to those from an age- and sex-adjusted, otherwise healthy population, to find that the GFR value of donors was 72% of that

Table 1. Summary of reviewed papers on long-term effects of donation on physical health.

Fehrman-Ekholm et al. Transplant, 2000; long-term Retro	No impairment of renal function, but 10% developed proteinuria.
Goldfarb et al. J Urol, 2001; long-term Retro	Creatinine and blood pressure increased but within normal ranges.
Ramcharan and Matas. Am J Transplant, 2002; long-term Retro	Kidney function and hypertension in donors are similar to those in persons in an age-matched population.
Schostak et al. Clin Transplant, 2004; long-term Retro	42% of donors felt they had a lasting impairment.
Gossman et al. Am J Transplant, 2005; long-term Retro	Bone metabolism changes and a high rate of proteinuria were detected.
Najarian. Transplant Proc, 2005; Review	Donors show good long-term survival and a high quality of life.
Torgay et al. Transplant Proc, 2005; Retro	Creatinine levels increased after donation but remained within normal range.
Boudville et al. Ann Intern Med, 2006; M-A	Within 5-10 years, the blood pressure of donors increases 5 mm Hg more than that expected from normal ageing.
Fehrman-Ekholm et al. Clin Transplant, 2006b; Retro	ESRF rates among donors was similar to those expected in patients in an age-matched population
Garg et al. Kid Intl, 2006; M-A	Small increase in urinary protein and an initial fall in GFR.
Weitz et al. Clin Transplant, 2006; Review	Living donor kidney transplant has an acceptable risk-benefit ratio.
Azar et al. Transplant Proc, 2007; Retro	Total complication rate was 55%, and serious complications occurred in 6%, concluding that donation is not very safe.
El-Agroudy et al. BJU Intl, 2007; Retro	Renal function is maintained and donation has a minimal complication rate.
Housawi et al. Neph, Dial, Transplant, 2007; Questionnaire	Inconsistency in the risks communicated to donors about long-term risks of donation.
Sahay et al. J Assoc Ind Phy, 2007; Retro	Compared to predonation values, a rise in blood pressure and proteinuria and a fall in GFR were found.

Abbreviations: ESRF, end-stage renal failure; GFR, glomerular filtration rate; M-A, meta-analysis; QoL, quality of life; Retro, retrospective follow-up study.

expected from healthy subjects (SD=18) (14). Both studies found no correlation between GFR and time since donation, implying that there is no further deterioration of GFR other than what is expected from ageing alone.

Microalbuminuria and proteinuria

Detection of microalbuminuria is used as an early marker of subclinical renal injury, particularly in

diabetics. Proteinuria is also useful in monitoring the progression of renal failure (10, 18). In a follow-up by Fehrman-Ekholm 12 years after donation, proteinuria of less than 1.0 g/L was found in 9% of donors; 3% had significant proteinuria (> 1.0 g/L). Of the 10 donors who had significant proteinuria, 9 had their nephrectomy before 1982, but the study reviewed nephrectomies until 1995 implying that over time, the incidence of proteinuria had decreased (14). The Gossman and associates study mentioned earlier found that 56% of donors have proteinuria of more than 150 mg/day, but only 10% had abnormal urinary albumin concentrations above 50 mg/L (0.05 g/L). This was much higher than those found in the Fehrman-Ekholm study but could be partly accounted for by different methods of measurement. Measuring more specific marker proteins, 10% had abnormal urinary albumin concentrations (> 0.05 g/L), 7% had increased urinary α 1-microglobulin suggesting tubular injury, and 2% had abnormal IgG excretion signifying glomerular disease (15). A meta-analysis found the pooled incidence of proteinuria from 42 studies to be 12% at an average of 7 years after donation (17).

After varying conclusions made from several studies, the association of proteinuria with hypertension is questionable. However, most trials conclude that proteinuria is not progressive with time after donation and acknowledge that further follow-up is needed to check the clinical significance of these rates (14, 15).

Hypertension

It has been proposed that the reduced number of glomeruli after nephrectomy causes hyperfiltrative damage to the remaining kidney resulting in hypertension (18). Gossman and associates found that the number of donors with hypertension rose from 7% before donation to 30 percent 11 years after donation ($P < .001$). This involved a significant rise in mean systolic blood pressure from 125 ± 15 to 134 ± 19 mm Hg ($P < .001$) and a nonsignificant rise in diastolic blood pressure from 79 ± 11 to 81 ± 9 mm Hg (15). Similarly, in the Fehrman-Ekholm study, hypertension was prevalent in 38% of donors 12 years after donation (14). Hypertension was defined in both studies as a blood pressure above 140/90 mm Hg or treatment with antihypertensive medicine. In both studies, however, the prevalence was significantly lower than that in age-matched normal

populations. This is somewhat expected, because donors are selected for having normal blood pressure. However, for the small number of donors that do have hypertension, it is impossible to determine whether the hypertension would have developed without donation. Gossman and colleagues also concluded that blood pressure did not correlate with proteinuria, GFR, age, sex, body mass index, or smoking status, variables that it does correlate with in healthy persons (15).

Boudville and associates conducted a meta-analysis focusing on the risk of hypertension in kidney donors. Of the 48 studies analyzed, there was only a limited number of studies at a minimum of 5 years after donation that used control participants who were healthy volunteers or people who were being evaluated as potential donors who were of similar age, sex, race, and height distributions as were the donors. The weighted mean increase in donor systolic blood pressure from 4 controlled studies was 6 mm Hg (95% CI, range, 2-11 mm Hg). Similarly, the mean increase in diastolic blood pressure from 5 controlled studies was 4 mm Hg (95% CI, range, 1-7 mm Hg). Therefore, Boudville and associates estimated an increase of 5 mm Hg in the blood pressure of kidney donors 5 to 10 years after donation but stressed the need for further controlled, prospective studies for more-accurate calculation. Although the increases in blood pressure noted initially seem small, it is worth remembering that every "10 mm Hg increase in systolic blood pressure and 5 mm Hg increase in diastolic blood pressure is associated with a 1.5-fold increase in death from ischemic heart disease and stroke" (13).

Comorbidities not related to nephrectomy

Most literature on kidney donor follow-up evaluates potential damage to the remaining kidney but does not thoroughly identify the occurrence of comorbidities. Some studies also exclude donors with comorbidities that are not related to nephrectomy; however, it is unknown how researchers decided that a comorbid condition is not related (18). Isolated findings from certain studies have been presented here.

Data on bone metabolism in kidney donors are scarce, but Gossman and associates measured some of its parameters, and as one would expect found a low level of 1α -hydroxylase after removing a kidney, resulting in secondary hyperparathyroidism. Although

elevated parathyroid hormone levels were found in 19% of donors after 11 years, they were not correlated with decreased 1,25 (OH)₂ vitamin D₃ levels. Parathyroid hormone levels increase 1 α -hydroxylase activity, and the authors suggest that there may be a new steady state of hormones existing here after the initial drop in 1,25 (OH)₂ vitamin D₃. To elicit the clinical significance of these findings, data on bone mineral density or fracture rates may be more helpful (15).

Schostak and associates assessed donors at a mean of 7 years after surgery and found that although 41.5% of donors felt they were adversely affected by the intervention, somatic problems (such as abdominal, respiratory, or scar problems) were only rarely found. Of the 102 donors targeted, only 53 responded, and it is likely that those with complaints were more willing to come forward and participate. Nevertheless, of the 53 donors, 14 had sensory disturbances, 4 had concrete complaints involving the abdominal organs, and 2 had problems involving the respiratory organs. Persistent pain was reported in 11 donors, occurring rarely in most but permanently in 2 (16).

The prevalence of diabetes mellitus in donors also has occasionally been noted in follow-up studies. El-Agroudy and associates found that it developed in 23 (6.8%) of the 339 donors evaluated at an average 10.7 years after donation. The authors found no correlation to age or interval after donation. Furthermore, this incidence was significantly lower than the incidence of diabetes mellitus in the age- and sex-matched population ($P = .01$) (8). Another study found 19 of 250 donors developed diabetes 6 to 34 years after donation, 10 of whom had a family history of the disease (19).

Mortality and renal failure

Death due directly to kidney donation is rare and mainly occurs due to operative complications. However, the question arises whether kidney donors have a reduced lifespan or are more likely to die of renal failure in the long term. A follow-up study by Fehrman-Ekholm and associates found that 49 of the 451 donors had died after 12 years, but none died of renal disease, end-stage renal failure, or ever needed dialysis. The majority of deaths were due to cardiovascular diseases and malignancies (14). Similarly, in the study by Gossmann and associates, after 11 years, the 7 deaths out of 152 donors all were due to these 2 causes (15).

However, mortality due to cardiovascular disease or malignancy is common in the general population too. One study found a significantly lower incidence of cardiovascular morbidity in kidney donors than in age- and sex-matched persons in the general population at a mean follow-up of 10.7 years after donation (3.2% vs 6.2%; $P = .04$) (8). Most trials conclude that there were no deaths due to renal causes; however, nonrenal causes are generally not detailed or followed up thoroughly to allow any significant conclusions about their likelihood after donation (3, 18).

Studies have not shown that kidney donors have a shorter lifespan. On the contrary, there have been suggestions and data published stating that kidney donors live longer than do age-matched persons in the general population. The cause of this, however, is likely to be the positive selection of healthy volunteers for donation as well as the more-frequent health follow-ups donors receive (15, 20). A follow-up study by Narkun-Burgess and associates concluded that compared with their fellow veterans of the same age, 56 World War II veterans who lost a kidney owing to trauma did not have increased mortality 45 years later (8, 19, 20).

A study by Ramcharan and Matas attempted to follow up kidney donors in the long term, 20 to 37 years after donation. Although a few donors had developed renal insufficiency and end-stage renal disease, the majority had normal kidney function. Percentages of proteinuria and hypertension also were similar to the age-matched population. Goldfarb and associates also examined donor renal outcome after 20 years or more. They concluded that renal function was well preserved, and that although creatinine levels and systolic blood pressure had risen significantly ($P < .001$), these values were still within the normal range. The prevalence of hypertension at 48% was comparable to the prevalence in the age-matched general population (21). Similarly, in a retrospective analysis of 1112 consecutive living donors, only 6 (0.5%) developed end-stage renal disease at median follow-up of 20 years, which is similar to the time expected in persons in an age-matched general population (22).

Donor follow-up in developing countries

The effects of kidney donation in different countries could vary owing to unique genetic backgrounds and ethnicities as well as environmental factors (18).

Most of the trials reviewed above were done in developed countries. But now, the results of 2 studies from developing countries show differences in donor outcomes.

Azar and colleagues, in Iran, evaluated 86 donors at a mean of 17.24 months since nephrectomy. No patients died, but there was a complication rate of 54.6% including hypertension in 37.5%, half of whom had a positive family history for the disorder. Although renal function was normal before donation, 6 patients had a serum creatinine level of 1.4 mg/dL or more after the nephrectomy; microalbuminuria was observed in 9 patients and hematuria was observed in 12. The authors claimed to have observed a higher rate of donor hypertension and proteinuria compared with other studies and concluded that donation is "not so safe."

A more thorough and expansive article by Sahay and associates was published in February 2007 looking at the "Indian Perspective." Fifty donors were followed up at a mean interval of 63 months after nephrectomy, at which time 22 had developed hypertension; these included 7 donors who had a positive family history of hypertension. Twenty of the donors developed microalbuminuria, and 7 developed overt proteinuria. There were significant reductions in GFR and increases in renal length after nephrectomy ($P < .05$), but the changes in the creatinine levels were nonsignificant. Although there were no donor deaths related to nephrectomy, hypothyroidism developed in 1 donor, and type 2 diabetes mellitus developed in another. The Sahay and associates study confirmed the safety of live kidney donation and compared the findings with those from the West. The study by Sahay and associates concluded that Indian donors do not respond any differently after nephrectomy than do their Western counterparts. However, hypertension and renal function seemed to be more severely affected in Indian donors than in donors in the Western meta-analyses mentioned in the study (18).

Long-term psychological effects of donation (Table 2)

The psychological basis of why healthy donors are willing to risk their lives to help a fellow person has long been studied. Is it material gain, family pressure, or an altruistic desire? This abstract phenomenon has caused many countries to have strict donation regulations.

Table 2. A summary of reviewed papers on the long-term psychological effects of donation.

Johnson et al. Transplant, 1999; Retro	Donors scored higher than the national norm using the SF-36 Qol questionnaire
Papalois and Matas. Curr Op Organ Transplant, 2000; Review	Donation had positive effect on donor-recipient relationship
Franklin et al. Transplant, 2003; Questionnaire	Decision to donate is difficult and can lead to conflict within a family
Jordan et al. J Nephrol, 2004; Retro	Majority would donate again and were satisfied with treatment received
Clemens et al. Am J Transplant, 2006; Review	Harm can be minimized through careful selection and follow-up

Abbreviations: Qol, quality of life; Retro, retrospective follow-up study.

One study found that before surgery, donors were more content, reported fewer psychiatric problems, and felt more strongly that life was worth living compared with persons in a control population (23). A British cohort study found that 6 weeks after surgery, donors' SF-36 quality-of-life questionnaire scores decreased but were still significantly higher than scores for persons in the control population. Compounding this decrease in well-being after donation, 1 study found 23% of donors admitted feeling depressed after surgery. However, in the longer term, donors who see the recipient obtaining an enhanced quality of life gives psychological strength to the donor and can enhance self-esteem (24).

The majority of donors are relatives of the recipient, and donation can affect their relationship. A systematic review of the psychosocial health of donors by Clemens and associates, indicated that overall, between 86% to 100% of donors either had an improved or unchanged relationship with the recipient (23). In addition, 68% of parental donors felt it was "true" or "very true" that the relationship with their child had improved after donating to them. Siblings have a complicated decision, as it includes altruism, manipulation of social dynamics, and the guilt of refusal (25).

Another study looked into the psychological status of German donors after an average of 11 years (26). The researchers found that 97% of donors would donate again, and 91% of the donors were satisfied with their decision. However, in those cases in which the recipient had not survived, 50% of the donors believed the procedure was not worth it, and 43% said the graft failure had left a feeling of guilt and bitterness. In addition, 11% of these donors had had

suicidal thoughts (23). This could be due to the donor feeling directly responsible for the graft failure and having an increased sense of helplessness. Another study concluded that donors whose recipient had died had lower scores on the quality-of-life questionnaires compared with donors whose recipient had not died; however, scores of donors whose recipient had died on the quality-of-life questionnaires were still equal to scores from persons in the general population (27).

Conversely, 33% of donors who were not close to the recipient previously felt that the surgery had negatively affected their life compared with 8% who had had a close relationship before the surgery. However, 83% of those who had had a close relationship would still strongly encourage others to donate (2). Johnson and associates found that the risk factors for a poor psychosocial outcome were non-first-degree-relative donors and donors whose recipient had died within a year (24). Thus, a correlation was found between psychological outcome and closeness to the recipient, a finding that questions the decision of countries who are against donation within relatives. Samaritan donors are those who donate to patients they do not know. They go through more rigorous psychological evaluation than a related donor (28). There are potential psychological benefits to this, because anonymity is reserved for both donor and recipient unless there is a mutual agreement to meet; thus, there is less emotional attachment for the donor after donation. Therefore, there is no guilt, bitterness, or helplessness if the graft were to fail as mentioned before. On the other hand, the Samaritan donor does not gain the boost of self-esteem that a known donor would.

Relationships other than those between the donor and recipient can be affected. One study found that only 2% of donors stated that the kidney donation procedure had directly upset a relationship in their life. In 1 instance, a female donor divorced her husband because he had withdrawn from donating to their child. Similarly, a donor felt disappointed with a sibling who decided not to donate to another sibling (26). Both of these cases show that the decision to donate had an effect on another relationship besides that between donor and recipient. Additionally, 33% of donors who had since divorced cited donation as the reason, but the divorce rate of donors was still lower than that of the general population (23). Many health care systems demand a

psychological consultation of the patient; however, no standards have been set.

Therefore, donating has a psychological effect, and evidence suggests there should be a routine protocol for evaluating donors to ensure that those more vulnerable to depression are given the necessary advice. Making decisions regarding donation in addition to the pressures of caring for the recipient and one's self can all conspire to bring about depression. This would be particularly significant in a parent-child relationship. Furthermore, financial worries can add to an already stressful situation, because donors will need time of work and some may feel they are unable to get medical insurance, even though a survey of American insurance companies found a majority of health care organizations did not raise their premiums for healthy donors (29).

Long-term effect of donation on quality of life (Table 3)

Table 3. A summary of reviewed papers on long-term donor quality of life.

Isotani et al. Urol, 2002; Retro	Qol unaffected, but calls for better psychological preparation of donor
Chen et al. Transplant Proc., 2004; Retro	Risks of donation are low, and donors were more concerned about cosmesis

Abbreviations: Qol, quality of life; Retro, retrospective follow-up study.

The World Health Organization has defined quality of life as the physical, psychological, and social domains of health (29). Thus, health is more than just the absence of disease, and clinicians must understand how much surgery affects a patient's way of life. Studies have found that preoperative quality of life is regained only 1 year after surgery (30).

Donors scored higher than did persons in the general population in physical function, bodily pain, and mental health aspects of a quality-of-life survey; however, the difference was not statistically significant (31). Body image is important with regard to returning to a normal quality of life. The authors of a Taiwanese study found that donors were generally happy apart from the cosmesis of their scars. The donors who had major problems underwent wound revision (32). A review mentioned 10 studies that evaluated the body image of donors; 2 studies found no meaningful change in appearance, although

interestingly, data from 1 of these studies showed that 15% of those surveyed thought that the scar increased attractiveness; only 2% perceived themselves as less-attractive in front of their partner (23).

Clemens and associates found a generally positive donor response from the systematic review they performed. Quality-of-life investigations found that 95% of the donors had no change after donation. There was a significant decrease in scores for the mental health components of the questionnaire between 4 and 12 months after surgery; however, this decrease was not below that of persons in the general population (23).

Discussion

In the long term, kidney outcome measures have indicated reduced renal function after donation, but figures tend to remain within normal ranges and are consistent with those of persons in age-matched populations. Furthermore, studies have not shown an accelerated loss of kidney function after donation or increased chances of renal failure after donation.

Although studies show an increase in blood pressure after nephrectomy, the prevalence of hypertension is still lower in donors than it is in persons in the general population. Meta-analyses of controlled studies have found a slight increase in blood pressure for donors in the long run that could contribute to higher cardiovascular risks. This rise in blood pressure can be monitored and controlled with medication at an earlier stage. Angiotensin converting enzyme inhibitors and angiotensin 2 antagonists have been suggested, but no controlled trials have proved them to be the best treatment in kidney donors (22).

No disease has been firmly associated with kidney donation, and donors do not have a reduced lifespan; on the contrary, donors have been found to have longer lives perhaps owing to the selection of healthy volunteers. Follow-up studies of donors from developing and developed countries have found similar changes in renal function and blood pressure, however, these have been shown to be more pronounced in developing countries. However, only a few studies have been compared in this review, and outcomes are likely to vary between countries and health centers. Hence, to draw significant conclusions on this matter, a more-

extensive comparative study is necessary. Overall, the studies have mostly confirmed the long-term safety of unilateral nephrectomy, although all have stressed consistent follow-up of donors for research and health monitoring purposes.

The motivation and psychological status of donors needs careful assessment by dedicated social workers, counselors, and psychologists. Donors should be fully informed of the procedure and be able to raise concerns and discuss in confidence any issues that may arise. Follow-up also should take place because studies have shown that between 4 and 12 months after surgery, there is a decrease in the mental health of donors (23). Furthermore, if the graft fails or the recipient dies, resources should be available to counsel the donor and secure their mental health.

Studies have shown that donor outcome is better if the recipient is a first-degree relative, but this is restricted in countries where relatives are not allowed to donate. Allowing relatives to donate could increase the number of kidneys available for donation in such countries. To ensure that the donor is not acting impulsively and fully understands the risks (otherwise, donation could prove psychologically damaging), it is important to address the factors that motivate relatives to donate kidneys.

Live kidney donation is an evolving practice, and various modifications have occurred since it was introduced. Therefore, older studies may be misleading because of changes in selection criteria and surgical technique. For that reason, we have included only those studies done between 1993 and 2008 for this review. Nevertheless, we have cited some studies that follow-up donors for periods over 20 years and such long running studies tend to have difficulties with compliance. In the Ramcharan and Matas study (20) (20- to 37-year follow-up), information was available only for 464 (60%) of the 773 donors, and laboratory test results were available for only 125 (15%), while Goldfarb and associates (21) managed to follow-up only 70 (38.8%) of the donors assessed in a study 20 or more years after donation. Because most of the nephrectomies were done between 1963 and 1975 in both studies, it is likely that techniques and complication rates have improved over time, and that donor selection criteria have changed significantly. The low participation rates noted here are characteristic of studies on kidney donor outcome, making it difficult to form

conclusions. In addition, retrospective studies are susceptible to bias and incomplete data. Thus, efforts must be made to increase participation in follow-up studies.

As mentioned by Ommen and associates, careful appraisal of available data is required so that valid information is available to physicians and potential donors. A key area highlighted is the use of controls in donation studies. A comparison is usually made between donors and persons in the general population. Studies finding that the physiological outcomes of donors are similar to or better than those of the general population must be scrutinized, because donors are expected to be healthier than persons in the general population before donation as they must meet certain selection criteria. Many long-term studies have small sample sizes, and thus, the "negative results" found may simply be the result of underpowered studies. This can be misleading, and greater efforts are needed to ensure that long-term studies are not underpowered (33).

Different centers use different selection criteria. This implies that selection criteria are not universal and with ever-increasing demand, these criteria continue to expand. A study is needed to determine modern, safe inclusion criteria for donors, otherwise overcautious or unsafe practices will continue.

Quality long-term studies examining the health risks of kidney donors also would improve donor care. Worldwide, there is a need to tend to the needs of living donors and increase their safety (6). This can be done at various stages of the donor's "journey," starting with the decision to donate. Providing informed consent is crucial, with the donors receiving information not only about the risks and benefits to themselves and the recipient but also about alternative treatment available to the recipient (10). In addition, the donor should be able to assess the outcomes of the transplant center performing the operation (34). A recent study by Housawi and associates (35) found that transplant professionals vary in the long-term risks they communicate to potential living donors. This stems from uncertainty on the part of the professional regarding long-term risks. Hence, quality follow-up of donors is crucial for improving donor selection criteria and providing the best estimates of potential risks to potential donors (13, 35).

Because of the long-term medical risks donors face, there is significant need for lifestyle changes;

this increases the need for long-term follow-up of the donors (13, 35). Almost all papers consulted for this review stressed the need for structured long-term follow-up of donors for both health monitoring and research purposes. Fehrman and associates (14) suggest that check-ups every 2 to 3 years could be done by general practitioners including measurements of s-creatinine, blood pressure, and a urine test for proteinuria. Donor registries are an important way to summate and monitor donor health. In the United Kingdom, the Living Donor Registry was set up in 2000 and should be used by other countries such as India where the program has not yet begun (18). Ultimately, this could lead to a world donor registry.

Further proposals to protect donors include reimbursing donors for any expenses they incur. This may involve costs for time taken off from work and for the costs of travel costs for the donation itself, as well as reimbursement for antihypertensive therapy or higher insurance premiums donors might have in the long term (6, 13). Such payments differ from financial gain, and along with improved donor care, can encourage more people to donate.

To resolve a deficit of organs, there needs to be a sensible expansion of donor criteria along with improvements in surgical and medical care. Current guidelines such as those from the Amsterdam forum should be used, and all donors should have standard tests to assure their safety (36). Thorough donor investigations can identify and exclude high-risk donors, for example, those with hypertension or deteriorating renal function. This could include a family history and in the future, genetic screening if a valid test becomes available. A good example of how donor exclusion criteria have been relaxed successfully and have been combined with advances in medical therapy is ABO-incompatible donation. With improved immunosuppressive drugs, ABO incompatible donation has been shown to yield similar results to compatible donations in the short term. Some UK centers predict an increase in living donation of 10% to 20% as a consequence.

Mandelbrot and associates (37) investigated changes in the selection criteria of living-kidney donors in the United States between 1995 and 2007. They concluded that exclusion criteria had become less strict to compensate for the increase in living donation in this period. A greater proportion of centers had no upper age limit for donation; however, most implemented a

lower age limit of 18 years old. There was still no clear guidance for some investigations, for example screening for glucose intolerance; thus, it is felt that clear standardization is needed.

In conclusion, live kidney donation does not have a major detrimental effect on the health of the donor. Although renal function and blood pressure may worsen slightly, levels remain comparable to those of age-matched persons in the general population. Most donors are happy after donation and would, in hindsight, donate again. With improved surgical techniques and medical therapy, live-donor transplant is set to be used even more frequently. However, there is a clear need for a more-thorough and structured follow-up protocol for donors to ensure optimal care as well as for research purposes to provide increased information to help safely expand the donor pool.

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