

*Editorial Comment*

**Risks in life after living kidney donation**

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Kidney transplantation, particularly from a living donor, is considered the treatment of choice for selected patients with end-stage renal disease (ESRD). A successful transplantation not only provides a better quality of life but also a survival advantage to the transplanted patient [1]. The superior results which can be achieved with kidney transplantation from living donors and the limited supply of organs from deceased donors are the two major reasons for the increase in living-related kidney transplantation in the USA, Europe and worldwide in the past 30 years [2, 3]. When compared to deceased donor transplantation, living donor kidneys not only provide better long-term patient and graft survival rates but also result in shorter wait times on the waiting list as well as an opportunity for early or even pre-emptive transplantation [4]. Most conveniently, transplant surgery can be performed electively during daytime and the graft usually shows initial function postoperatively. As living kidney donation began to gain wider acceptance in all transplant centres, there was an enormous concern in terms of safety for the donor beginning with the medical evaluation prior to kidney donation, the risk of the operative procedure itself and the long-term medical and psychosocial consequences of uninephrectomized patients. Since the data available on the long-term medical outcomes in a complex situation such as kidney donation is still limited, the manuscript of Lam *et al.* [5] in the current issue of this journal about the risk of acute dialysis in living kidney donors further contributes to our understanding and risk assessment when dealing with living kidney donation. They assume that a reduced kidney function confers a higher risk of acute kidney injury in different settings such as sepsis and try to find an answer whether this is true for those patients with reduced renal mass after living donation. In their population-based matched cohort study, Lam *et al.* reviewed the medical records of living donors from 1992 to 2009 and linked the information with health care databases to compare the risk of acute renal failure of 2027 living donors with that of the normal population (20 270). In this particular study, the observed rate of acute dialysis did not show any significant difference between kidney donors

and the normal population and therefore can be reassuring in relation to the practice of living donation in terms of risk for the donor.

Nevertheless, it needs to be emphasized that it is mandatory to make living-related kidney transplantation as safe as possible for both the recipient and the donor. Therefore, it must be ensured that every prospective living donor has to undergo a thorough medical, psychological and social evaluation prior to kidney donation, as recommended by the Amsterdam Forum [6].

**Donor evaluation**

What are the parameters we need to look at prior to kidney donation? It starts with an adequate kidney function with an acceptable glomerular filtration rate (GFR) which is an essential prerequisite for good kidney function post-donation. It is therefore necessary to accurately measure GFR in potential donors for risk assessment. Consequently, most transplant centres have set a GFR cut-off (80 mL/min/1.73m<sup>2</sup>) only above which a living donation is realized [7]. In addition, obese donors have to be thoughtfully evaluated and educated since obesity is an accepted risk factor for kidney function either as a direct result of being overweight or indirectly because of the associated comorbidities, such as hypertension, diabetes or hyperlipidaemia [8]. Obese patients also have a higher risk of perioperative complications and as a result, many transplant centres exclude overweight patients, e.g. with a body mass index (BMI) >35kg/m<sup>2</sup> for donation [9].

Because of the increasing demand for organ donation, the eligibility criteria for living kidney donation has been extended recently to generate a larger pool. These potential donors are called extended criteria or medically complex donors, defined vaguely as donors of older age, obese, with controlled hypertension, microscopic haematuria, nephrolithiasis or even microalbuminuria [10]. For most of those donors, e.g. older donors above the age of 60 years, long-term results are not yet available [11]. With every potential donor presented to us, we therefore have to ask ourselves two crucial questions: firstly, whether the donor is fit enough for the surgical procedure and secondly, how willing we are to accept a medically complex living donor. To date, no particular guidelines exist which define the margins for

certain parameters (e.g. GFR, BMI, hypertension, age, comorbidities) within which living-related kidney donation is regarded to be safe. Besides the general recommendations as stated in the Amsterdam Forum, it is still only the responsibility of the nephrologist and surgeon to accept or reject a kidney donor. Since considerable differences exist between countries and even among transplant centres in the evaluation and selection criteria for kidney donors, especially in complex patients such as older donors and those with associated comorbid conditions, it is necessary in the future to discuss, redefine and establish minimal selection criteria for living kidney donation.

### Short-term outcome

Regarding short-term morbidity and mortality, there are numerous excellent studies available describing perioperative risks. In general, the operative procedure is well tolerated, standardized and relatively safe, independent of whether the kidney is removed by open or laparoscopic surgery. The major morbidity of the procedure is up to 5% and the overall morbidity is up to 15% [11]. Although low, there is a potential risk of harm to the donor. Matas *et al.* [12] found two donor deaths (0.02%) from surgical complications, both after laparoscopic donation, and the United Network for Organ Sharing data revealed a surgical mortality from kidney donation of 3.1 per 10 000 donors [13]. These are figures both physicians and potential donors need to be aware of prior to living donation and particular prior to the operation.

### Long-term outcome

There are several aspects to be considered regarding living kidney donation and long-term renal consequences. It must be noted that true long-term outcome data are rare since there are relatively few donors from 20 to 30 years ago. In general, the lifespan of kidney donors and their health status and quality of life correlate to their morbidity post-donation, mainly influenced by their renal function. Hypertension and diabetes are the leading causes of ESRD [14]. Ibrahim *et al.* [15] found that the risk of hypertensive donors post-donation is increased with age and with a higher BMI. But at the same time, both hypertension and diabetes developed at a similar frequency among donors as in the general population [15]. In 1997, Fehrman-Ekholm *et al.* [16] even postulated that 'kidney donors live longer'. At least many studies have confirmed that life expectancy of kidney donors as well as the risk of ESRD seems to be comparable to that of non-donors. In concordance, reports of long-term follow-up after nephrectomy of one kidney suggest that the removal of one kidney does not affect the survival or the function of the remaining kidney in an otherwise healthy person [17].

Nevertheless, the most dramatic complication in long-term follow-up for donors is undoubtedly to suffer from ESRD themselves. Gibney *et al.* [18] found a risk for need of a kidney transplantation after kidney donation of 0.1% after a mean time of 17.6 years after donation (102 of 51 308

donors from 1993–2005). The main reasons to be listed on the kidney waiting list were hypertension, focal-sclerosing glomerulosclerosis and diabetes. Rare risks were tumours, fibromuscular dysplasia or trauma of the remaining kidney. Fortunately 'only' 11% of those 102 donors suffer from ESRD within 5 years after donation, while the majority of 60% are faced with ESRD >16 years after donation. Admittedly, this does not help the donor who is <60 years. As mentioned by the authors, in addition, abdominal or retroperitoneal trauma as another risk for ESRD after donation is serious but rare. In addition, the urological therapy for renal trauma has evolved over the last decade, so that most traumata can be managed successfully in a conservative manner [19].

Focussing on other studies, the risk of ESRD does not seem to be elevated in kidney donors in comparison to the normal population. Fehrman-Ekholm *et al.* [20] reported a risk of 0.5% in 1112 kidney donors, which was similar to the Swedish population at the same time. The same holds true for other countries: Okamoto *et al.* discovered an incidence of 0.49% in Japanese donors ( $n = 601$ ) and Ibrahim *et al.* described a risk of 0.2% in 3698 cases in the USA [15, 21].

Whatever the originating disease for developing ESRD after kidney donation is, it is correlated with a loss of GFR. Garg *et al.* [22] have shown in their meta-analysis that 10 years after donor nephrectomy, the GFR of donors was 10 mL/min lower than the GFR of controls. A total of 12% developed a GFR <60 mL/min during follow-up. However, after the initial decrement in GFR after nephrectomy in their study, there was no evidence of an accelerated loss in GFR higher than that anticipated with normal ageing. This supports the view that risk factors linked to a reduced GFR in donors are the same as those that have been found in the general population.

The same group has now evaluated the need for acute dialysis in critical situations after kidney donation, which is presented in the current issue of this journal [5]. It is well known that reduced kidney function is a risk factor for acute renal failure in sepsis [23]. But this does not hold true for kidney donors post-donation as shown in the current paper. Technically and statistically, the survey is well done, using databases of the public health system combined with manual review of patient charts. With a mean follow-up of 6.6 years and a very low rate of loss to follow-up (<6%), the presented data seem reliable. As all transplant centres promote living donation due to the persisting lack of diseased donors, we must have a better understanding of the long-term living donor outcomes. Fortunately, this study provides an important safety data in this regard. Although an even longer follow-up and an evaluation of milder forms of acute kidney injury would be desirable, this new study of Lam *et al.* is of high interest to the transplant community regarding public trust in living donor kidney transplantation.

### Concluding comment

The health of a donor for living-related kidney transplantation is paramount. From an ethical viewpoint, donors

should be made aware of the risks and how lifestyle can affect these risks early on. It is crucial to carefully screen donors and essential to resist compromises. If this is respected the survival, the comorbidity, ESRD or even acute renal failure, as shown by Lam *et al.* in the current issue of this journal, appear to be similar to those in the general population. Generally accepted and evidence-based guidelines for living donor kidney transplantation would certainly help to minimize short-term and long-term risks for those who are willing to donate their kidney. And finally, we have to ensure that every single donor receives adequate medical care after nephrectomy. Long-term surveillance is essential and donors must be encouraged to attend follow-up clinics to modify risk factors, allow early intervention and to finally further develop evaluation criteria for optimizing donor selection.

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