





incorporates weighted donor and recipient factors in the top 20% to maximize kidney graft survival. A young patient with GN, for example, would be allocated a high-quality deceased donor organ with the highest estimated potential longevity. Such a patient near the top of the waitlist might fare almost as well with a high-quality DDKT compared with an LDKT from an older living donor; this knowledge may affect a potential donor's decision. Thus, the primary nephrologist can provide initial education to patients and their potential donors as part of a process of shared decision-making to help them choose the option best for them. This initial information can then be discussed in greater depth during transplant center-based education and counseling, such as on the level of tradeoffs (recipient benefits versus donor risks) facing the potential donor-recipient pair. Although the new system may help to reduce the survival differential between DDKTs and LDKTs for this top 20%, it is unlikely to have such an effect for those below 20% and fully eliminate the difference for those in the top 20%, because LDKTs will always have an advantage regarding shorter warm ischemic times than DDKTs.

## Timing of Living Donor Transplantation

One of the primary benefits of LDKT to recipients is avoiding the ever-growing wait time for DDKT. Donor-recipient pairs should be informed of the possibility of preemptive transplantation and may seek advice on this possibility. However, the optimal timing for performing preemptive kidney transplantation in relation to the recipient's stage of CKD remains controversial. There is strong evidence that preemptive transplantation offers significant advantages compared with transplantation after a prolonged period of dialysis therapy (9), and the amount of time spent on dialysis before transplantation seems directly related to increased mortality in a dose-dependent manner (10). However, some studies have raised questions about the mortality benefit to preemptive transplantation versus dialysis for a few months followed by transplantation (11). Specifically, if a preemptive transplant is performed too early, the half-life of the kidney may not be most wisely considered. For instance, if the kidney were to last 15 years and the patient receives the transplant 1 year too early, then 1 year of residual renal function is wasted, such that 15 years later, the patient needs another transplant. However, if the patient waits another 1 year until all residual renal function is entirely gone, then the patient would need another transplant 16 years later rather than 15 years later. Even among patients with advanced CKD preparing for dialysis, the benefit of early dialysis initiation remains inconclusive; the only randomized, controlled trial on the timing of dialysis and clinical outcomes found no differences in survival cardiovascular events, infections, or dialysis complications between early or late initiation of dialysis (12).

Countering the benefit of preemptive transplantation, there is also a poorly characterized potential increased risk of nonadherence with preemptive transplantation because of the fact that patients may be less motivated if they have not experienced the hardship and inconvenience of dialysis. In addition, potential kidney donors and their recipients should be informed about the risk of the longer cumulative immunosuppressive therapy that accompanies premature transplantation. Nonetheless, avoiding the inconveniences of dialysis and dialysis access surgery can be strong motivating factors for seeking preemptive transplantation, particularly given the incompletely defined long-term cardiac risks related to high-flow arteriovenous fistulas and quality of life benefits associated with transplantation.

Potential donors should receive education to address concerns regarding donation in the near future versus saving the kidney for donation at a later time. This issue is most likely to arise in situations involving younger patients with CKD, because their life expectancies are more likely to exceed their graft survival. A web-based calculator may aid in this process (13). Factors to consider in this decision-making process are that the potential donor may not be medically eligible for donation at a future time and that the recipient may become sensitized by a prior kidney transplant, causing an additional immunologic barrier to transplantation and rendering a previously acceptable donor ineligible to donate. The choice to donate and the timing of donation are ultimately in the hands of the potential donor, but nephrologists should provide donor-recipient pairs with this relevant information to inform this shared decision-making process.

## Risk Assessment and Counseling in LKD

Although there are substantial benefits to LDKT for the transplant recipient, as discussed above, there are also potential risks for the donor. The current OPTN policy on informed consent of living kidney donors outlines the elements of risk that must be disclosed as part of the informed consent process with living kidney donors, which are summarized in Table 2 (14). Our workgroup supports these policies and recommended expanding on them.

### Surgical Risks

The surgical mortality risk has been well studied, and it has been reported to be three per 10,000 patients (15,16). The rate has not changed over the last 15 years, a period that observed a transition from the predominance of open nephrectomy to laparoscopic nephrectomy. When counseling the potential donor, risk disclosure should provide surgical risks of living donation in the context of other types of surgical risks to help potential donors place donor risks into perspective. For example, Table 4 shows the surgical risk of mortality relative to other elective surgical procedures or medical events. In addition, donors should be made aware of stratified risk estimates on the basis of sex, race, and age (16), which will allow them to consider their own personal risk profile.

Procedure	Mortality rate (%)
Renal transplantation (LD)	0.0
Renal transplantation (GD)	1.0
Living donation (LD)	1.0
Living donation (GD)	1.0
Renal transplantation (LD)	1.0
Renal transplantation (GD)	1.0

Table 4.  
Surgical mortality of kidney donation compared with other procedures

## Long-Term Medical Risks

Potential long-term risks that have been most studied include risk of mortality, ESRD, and hypertension. Inferences from literature on these long-term risks are varied, because of the use of various control groups with which donors are compared and different periods of time that living donors and control groups are followed. The challenges in estimating the relative risk include the low event rate in kidney donors as well as the use of the appropriate comparison or reference group.

**Risks of ESRD and Mortality.** Prior studies had concluded that the relative risks of ESRD mortality and ESRD in kidney donors are equivalent to or lower than those of the (unmatched) general population (17,18). Among the general population, overall lifetime risk of ESRD for a middle-aged individual is 2.66% for men and 1.76% for women (19). In other words, approximately one in 40 men and one in 60 women of middle age will develop ESRD during their lifetimes. Although these conclusions have been largely reassuring, arguments have been made that risk assessment that compares living donors with healthy nondonors rather than the healthy matched general population is needed, because individuals with chronic diseases are generally excluded from donating.

There is emerging evidence of an increased long-term risk of advanced kidney disease after living donation, the extent to which varies by individual donor characteristics. The interpretation of this evidence remains controversial, but varying views should be made available to potential kidney donors. Two recent studies have, for the first time, compared donors with healthy nondonor controls rather than the general population. A study of almost 100,000 United States donors estimated that the lifetime risk of developing ESRD among kidney donors (90 per 10,000) is higher than in healthy nondonors (14 per 10,000) but lower than in the general population (326 per 10,000). In other words, approximately one in 100 kidney donors will develop ESRD compared with one in 30 in the general population and one in 700 in the healthiest nondonor population (20). It may help to clarify to potential donors that, compared with the general population, living donors have a lower risk of ESRD but that, compared with a healthy nondonor control group, living donors have a higher risk of ESRD. Similarly, a Norwegian study examining long-term renal function in living donors found that donors had a 30% increased risk of mortality and an 11-fold increase in ESRD compared with controls who would have been eligible for donation (21). Interestingly, in the Norwegian study, the primary causes for ESRD in donors who progressed to ESRD were predominantly from immunologic conditions (*e.g.*, GN and vasculitis) (21) and not low nephron mass *per se* (*e.g.*, secondary FSGS). Donors should be informed that the available studies have limitations, and specific issues that they should consider pertain to whether each of the study periods was long enough to fully capture progression to ESRD and whether deriving a single-donor risk estimate from a postdonation study can ever properly express the heterogeneity of actual risk (*e.g.*, between young and older candidates) (22). Although the intrinsic limitation to calculating accurate risk estimates in the setting of low event rates applies to these studies, these important cohorts provide additional information that would be helpful for potential donors in their decision to donate.

Donors should be advised that there are additional factors associated with risk variability, including comorbidities, long-term diabetic risk, family history, and obesity. Therefore, tailoring the potential long-term risk estimation to the individual donor on the basis of the donor's age, race/ethnicity, baseline GFR, and family history remains challenging. Risks are more predictable in older individuals; the medical evaluation of young potential living donors is less accurate in predicting lifetime risk of CKD (23). Similarly, racial/ethnic variability of risks exists as discussed below.

Donors should also be advised to adhere to good health maintenance practices and preventive care to mitigate the effects of modifiable risk factors of CKD. There is evidence that maintenance of a healthy lifestyle, maintenance of a healthy weight, exercise, smoking cessation, and adoption of a healthy diet can mitigate long-term risk (24). Opportunities should be sought to routinely educate donors in this regard both during and after the donation process.

**Racial Variation in Risk Estimates.** There are racial/ethnic variations in long-term risks of ESRD, hypertension, and diabetes (25) after donation. Relative to non-Hispanic whites, blacks have higher risks of ESRD (20), and both blacks and Hispanics have higher risks of hypertension after donation (26). Best strategies for screening potential living donors among individuals in these racial/ethnic groups remain controversial. Although recent genetic markers, such as APOL1, show association with development of kidney disease in nondonor populations, at present, there is no standardized screening approach. Potential donors with higher long-term postdonation risk should be strongly advised to receive regular medical attention to screen for and treat early hypertension.

**Hypertension.** Donors with preexisting hypertension have been increasingly accepted for kidney donation (27). In particular, select candidates with mild well controlled hypertension in lower risk groups (*e.g.*, older nonblacks) have been permitted to proceed with donation (28). Although the long-term cardiovascular and ESRD risks in these patients have not yet been fully evaluated, their short-term physiologic response to donation does not seem to

be maladaptive (29). In a longitudinal study of older living donors with a median follow-up of 6.3 years, adaptive hyperfiltration after donor nephrectomy was attributed to hyperperfusion and hypertrophy of remaining glomeruli rather than to glomerular hypertension (30). This suggests that aging donors with attentive follow-up medical care are unlikely to face accelerated progression of CKD. In the general population, hypertension is common with advancing age, and prospectively followed cohorts with primary hypertension but without hypertension resulting from another renal disease show little renal deterioration (31–33).

**Risks during Pregnancy.** In 2013, 16% of living kidney donors were women ages 18–35 years old (34), a population that has concerns regarding pregnancy after kidney donation (35). Complications of pregnancy (*e.g.*, preeclampsia, premature birth, and low birth weight) may be increased after donation. Some studies have concluded that kidney donors have increased risks of preeclampsia and gestational hypertension compared with matched nondonor controls (36,37). Recently, a retrospective study of pregnancies among kidney donors concluded that gestational hypertension or preeclampsia was more commonly diagnosed in kidney donors than in matched controls (11% versus 5%) (38). Although the absolute level of risk and the increment over that of matched controls may seem relatively low, potential kidney donors of childbearing age should be made aware of these data (38,39).

## Psychosocial Considerations

Numerous studies have shown that donors' quality of life after donation meets or exceeds that of other general population or nondonor comparison groups, and few donors regret having donated (40,41). Nevertheless, although the overall experience is positive for the majority of living donors, a variety of studies has suggested that some donors have unmet expectations and experience psychosocial problems, including emotional distress, changes in family dynamics, and psychosocial stressors. For example, the frequency of depression in kidney donors has recently been reported as roughly one in 10 within 5 years of donation (42). Although this is lower than that in the general population, it has not been directly compared with a nondonor population in any studies. A recent review noted that elevated psychologic distress and/or diagnosable psychiatric disorders have been documented in about one in four living donors, including incident cases in individuals with no predonation history of disorder; however, this information should be evaluated in light of the same limitations listed above (40). Finally, some donors report enduring worries about their current and/or future health because of their donation, and they may report persisting somatic problems, including fatigue and pain (40).

The relationship of these outcomes with donation is often unclear, because few studies follow donors from pre- to postdonation or include comparison groups of nondonors. Nevertheless, donors themselves have commonly described the onset or exacerbation of these problems as directly related to the donation. A preventive approach is optimal in most situations. For example, individuals receiving mental health intervention who are well stabilized before donation should continue care with their provider after donation; this may include continued pharmacologic agents, and continuity of care should be emphasized at the transitions.

Potential financial implications of donation, such as out of pocket expenses and future insurability effect, should be discussed with donors. These can constitute important burdens associated with donation, and they were discussed in more detail by another workgroup (43).

## Transplantation for Kidney Donors Who Subsequently Develop ESRD

Since the inception of LKD, the transplant community has acknowledged the altruistic nature of kidney donation and has been attentive to ethical concerns of justice. As such, the OPTN has a longstanding policy that gives priority in kidney allocation to prior living donors who require kidney transplantation. This policy's efficacy was recently examined by comparing the waiting time for kidney transplant and the organ quality of prior kidney donors who underwent kidney transplantation with those of matched nondonor cohorts under the standard allocation system (44). The study concluded that, compared with matched nondonors, prior living donors had a higher rate of DDKT, a shorter wait time, and lower post-transplant mortality, and they received higher-quality organs. However, this study only included prior living donors who were listed for transplantation; it remains unclear what proportion of living donors developed ESRD but were never waitlisted. Potential donors should be made aware of this policy and these reassuring findings and strongly counseled to seek transplantation evaluation should they ever develop ESRD.

## Conclusion

Donating a kidney is a unique opportunity for a healthy individual to make a profound contribution to another individual's health, but donation is not without risks. Although these risks can never be eliminated, the transplant community must work as hard as possible to estimate these risks and inform potential living kidney donors about them in a comprehensive and comprehensible manner. Education and risk disclosure are essential components of informed consent, which are necessary to ethically and legally justify living donation. Because recent and ongoing studies are adding significantly to knowledge regarding risks associated with LKD, this new knowledge should be expeditiously incorporated into donor educational materials and processes.

Key recommendations made by our workgroup are summarized in Table 5. The workgroup recommends that a living donor education toolkit be developed to facilitate comprehensive education for candidates and their potential donors. The toolkit should include information about the risks,

benefits, and alternatives to both the potential donor and the recipient as well as the donation procedures presented in a manner accessible to individuals with limited health literacy and numeracy. Risk calculators may also be particularly helpful in providing personalized estimates of individual donor's risks of death, ESRD, and possibly, hypertension and quality of life metrics as more data become available.

**Table 5.**  
Key recommendations for education of potential living donors

## Disclosures

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## Footnotes

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