1 Living Donation: The Gold Standard

Leonardo V. Riella and Anil Chandraker
Renal Division, Brigham and Women's Hospital, Harvard Medical School, USA

Introduction

The first successful transplant occurred in Boston in 1954, when a surgical team under the direction of Joseph Murray removed a kidney from a healthy donor and transplanted it into his identical twin, who had chronic glomerulonephritis [1]. The organ functioned immediately and the recipient survived for 9 years, after which time his allograft failed from what was thought to be recurrent glomerulonephritis. More than 50 years have passed since that breakthrough achievement, and transplantation has progressed from an experimental modality to standard of care. The introduction of immunosuppressive drugs such as azathioprine, prednisone, and later calcineurin inhibitors has led to better outcomes and, along with technical breakthroughs, expanded the pool of organs available to deceased and human leukocyte antigen (HLA)-mismatched donors.

Kidney transplantation has become the preferred therapeutic option for patients with end-stage kidney disease (ESKD), leading to better patient survival and quality of life. It is also more cost-effective than dialysis [2–4]. Unfortunately, the incidence of ESKD has risen steadily in the past several decades, creating a shortage of available organs for patients on the kidney-transplant waiting list (Table 1.1).

This growth in ESKD is related to the increased incidence of diabetes, obesity, and hypertension, combined with the improvement in treatment for concurrent health problems such as ischemic heart disease and stroke. The supply of organs from deceased donors has not followed the same upward trend, resulting in an ever-widening gap between eligible potential transplant recipients and available organs (Table 1.2).

In 2009, only 18% of patients on the waiting list for kidney transplantation received an organ [5]. The average waiting time for kidneys from deceased donors in the USA is more than 3 years, and in some geographic areas it is more than 5 years (Table 1.3)—waiting times that are sometimes longer than the average life expectancy of middle-aged and older persons with ESKD [6]. In line with these numbers, a recent study indicates that even

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Table 1.1 Waiting list for different organs in the USA. OPTN, Organ Procurement and Transplantation Network. Data from [5].

Waiting list candidates OPTN 2010	Number
All	107,075
Kidney	84,495
Pancreas	1,458
Kidney/Pancreas	2,182
Liver	15,948
Intestine	248
Heart	3,173
Lung	1,844
Heart/Lung	75

Table 1.2 Growth of the kidney-transplant waiting list compared to donor type in the USA. Data from [5].

	2009	1999	1989
Waiting List	84,495	40,825	17,786
All type donors	14,631	10,862	5,929
Deceased Donors	8,021	5,824	4,011
Living Donors	6,610	5,038	1,918
% Living donors	45%	46%	32%

Table 1.3 Time to transplant by organ type in the USA. Data from [5].

Organ type	Time to transplant in 2004 (median in days)
Kidney	1,219
Pancreas Transplant Alone	376
Pancreas after Kidney	562
Kidney-Pancreas	149
Liver	400
Intestine	212
Heart	166
Lung	792

major alterations in the organ procurement process cannot reasonably be expected to meet the demand for transplantable kidneys from decreased donors [7]. The imbalance between patient demand and the supply of organs from deceased donors has refocused attention on living kidney donors.

Epidemiology

Living-donor kidney transplantation is rapidly increasing in popularity worldwide and has surpassed the number of deceased donors in many transplant centers [5]. In 2009, approximately 40% of all kidney donations were from living donors, and most major transplant centers in the USA have been increasing the proportion of living donors, reaching more than 60% of total transplants in some. However, wide variations exist worldwide in the use of living and deceased kidney donors. These differences reflect varying medical, ethical, social, and cultural values, as well as the availability of deceased-donor organs. For example, Spain has possibly the most efficient system of deceased-organ collection, with less than 5% of transplants being from living donors. At the other end of the spectrum, strong cultural barriers in Japan have led to a preponderance of living-organ transplantation. Similarly, Turkey and Greece rely mainly on living donation as a source of organ transplantation [8].

Several factors have influenced the expansion of living donation. The advent of laparoscopic nephrectomy has reduced the associated morbidity of kidney removal, making more donors receptive to an interruption of the healthy course of their lives. Just as importantly, epidemiological data have shown that irrespective of the HLA match or the donor–recipient relationship, recipients of living-donor kidneys (LDKs) fare better than those who receive deceased-donor kidneys (DDKs) (Figure 1.1). Finally, the development of stronger immunosuppression and desensitization techniques has overcome many of the biological barriers to successful transplantation,

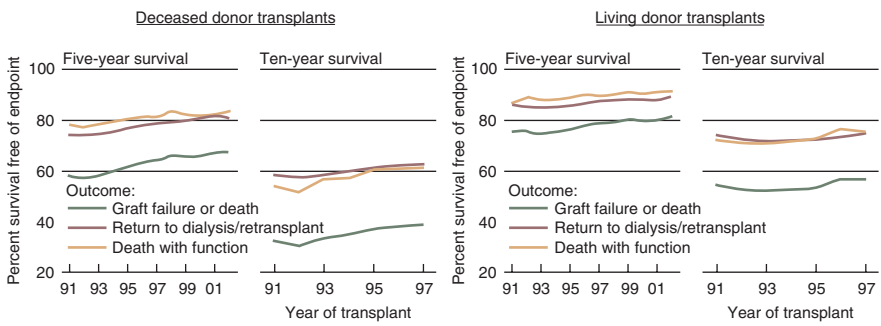

Figure 1.1 Outcomes of kidney transplants according to donor type. Graft-survival estimates are adjusted for age, gender, race, and primary diagnosis, using Cox proportional-hazards models. Conditional half-life estimates depend on first-year graft survival. (Reproduced from [6] The data reported here have been supplied by the United States Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the U.S. government)

such as ABO incompatibility or the presence of low to medium titers of antidonor HLA antibodies (Abs). Today, any person who is well and willing to donate may potentially be a live-kidney donor.

Advantages of living-kidney donation

It is well recognized that renal dysfunction is associated with accelerated heart disease. It has been estimated that mortality associated with cardiovascular disease is increased approximately 10-fold among patients with ESKD, even after accounting for age, sex, race, and the presence of diabetes [9]. Successful kidney transplantation progressively reduces the incidence of cardiac mortality and is therefore associated with an overall survival benefit in subjects undergoing kidney transplantation [10]. Even in older transplant recipients and patients with ESKD secondary to diabetes or obesity—subgroups with higher perioperative cardiovascular complications—survival benefits persist [4,11].

One-year survival for a functioning transplant is 90% for recipients of deceased-donor transplants and 96% for recipients of transplants from living donors. After surviving the first year with a functioning transplant, 50% of recipients of deceased- and living-donor transplants are projected to be alive with a functioning transplant at 13 and 23 years, respectively.

The waiting time on dialysis has emerged as one of the strongest independent modifiable risk factors for poor renal-transplant outcome [12], as can be seen in Figure 1.2. The presumed negative effect of prolonged dialysis is likely related to the impact of ESKD on cardiovascular morbidity and is observed in both living- and deceased-kidney recipients. However, even after a prolonged wait, patients who eventually receive a kidney transplant still have a lower mortality than those who continued on dialysis [13]. The possibility of undergoing preemptive transplantation without the need for dialysis gives the ESKD patients the best possible outcome [13–15]. With these observations in mind, until an optimal and timely source of organs is developed to decrease the prolonged waiting times, living-kidney-donor transplantation provides the best alternative for most patients [13–15].

Living-kidney donation is an act of profound human generosity and can be a source of much gratification for all parties involved. Many donors describe it as the most meaningful experience of their lives and the quality of life of donors after transplantation is reported to be better than or equivalent to that of controls [16]. Nonetheless, given the highly asymmetric nature of the physical benefits arising from kidney donation, a careful psychiatric evaluation of the donor is essential, to assess the coercion-free, informed, and autonomous decision to proceed with the process.

The number of sensitized recipients has increased dramatically in the past couple of years and these recipients usually face the greatest waiting times, due to the presence of preformed antibodies, and consequently have the greatest mortality. Desensitization protocols have enabled them to plan and receive an LDK at a determined time, but these protocols are expensive

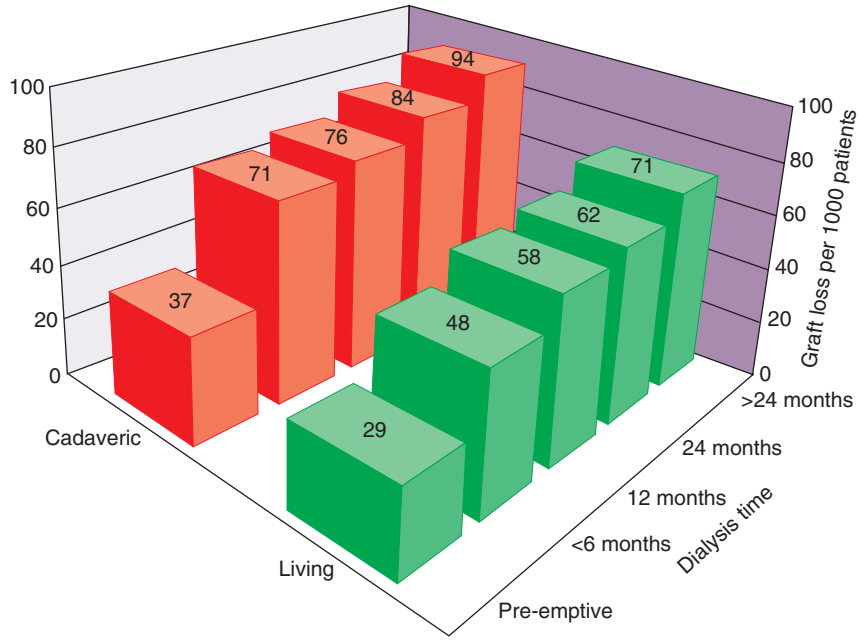

Figure 1.2 Comparison of rates of graft loss associated with living- and deceased (cadaveric)-donor transplantation according to time on dialysis prior to transplantation [12]. (Reproduced from [12], Copyright © 2002, (C) 2002 Lippincott Williams)

and labor-intensive, and in the USA have been implemented only for small numbers of patients. While successful in the short-term, the long-term outcomes remain unknown; these techniques are discussed further in Chapter 5. Another potential option for such patients is a paired-kidney exchange (PKE), which is discussed in more detail later in this chapter. For many years, immunological barriers were thought to be the largest hurdle in transplantation; today, many cite the acute shortage of organs as the major limitation.

Finally, the administration of donor-derived cells into the recipient in order to induce immunological hyporesponsiveness to the solid-organ transplant and minimize the need for immunosuppression has recently been explored. This hyporesponsiveness was thought to occur due to the generation of mixed chimerism, immune deviation, and/or generation of a regulatory immunological phenotype. Kawai *et al*. have recently published a report on a small number of successful cases of combined bone-marrow and kidney transplant in HLA single-haplotype mismatched, living, related donors, with the use of a nonmyeloablative preparative regimen. Four out of five recipients were able to discontinue all immunosuppressive therapy 14 months after transplantation, opening new possibilities for the induction of transplant tolerance with living-kidney donation, with consequent improvement in long-term outcomes [17].

In summary, living donation provides one answer to the shortage of donor organs, allows preemptive transplantation, and leads to better long-term

graft survival. It also permits the introduction of new, tolerogenic strategies, and for many donors will be a very positive and meaningful experience.

Types of donor

Related versus unrelated donors

Whereas rates of kidney transplantation from living related donors increased during the 1990s, transplantation from living unrelated (including spousal) donors has increased rapidly over the past decade, now accounting for nearly one-quarter of all transplantations from living donors in the USA (Figure 1.3). In 1995, a landmark report by Terasaki and colleagues documented that HLA-mismatched spousal transplants resulted in a graft survival superior to that of anything but identically matched kidneys from deceased donors [14]. This observation has influenced decisions regarding the suitability of live donors who are spouses, friends of the recipient, or anonymous; there is little concern today about the degree of HLA matching for the crossmatch-negative recipient of a kidney from a living donor. With directed donation to loved ones or friends, concerns have arisen about the intense pressure that can be put on people to donate, leading those who are reluctant to do so to feel coerced. Donor evaluation by a team of physicians other than that treating the recipient and a focus on the donor's interests when evaluating for donation minimize these risks. Furthermore, the general approach of simply reporting an unwilling donor as 'unsuitable' is a safe method of protecting the donor's decision without harming their relationship with the recipient.

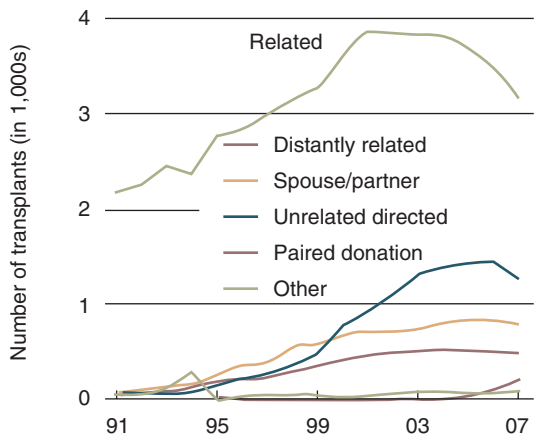

Figure 1.3 Number of transplants from living donors, by donor relation. (Reproduced from [6] The data reported here have been supplied by the United States Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the U.S. government)

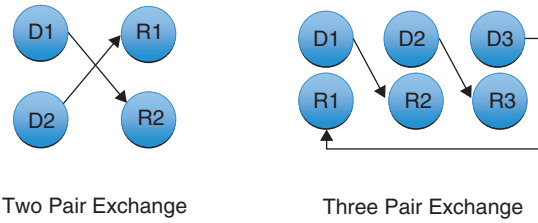

Figure 1.4 Examples of paired-kidney exchange (PKE). The traditional two-pair exchange is shown on the left, while a more complex three-pair exchange is shown on the right. The latter occurs when one of the donors is incompatible with the reciprocal matched recipient. The three pairs can be arranged so that donor kidneys are simultaneously exchanged from pairs 1 to 2, 2 to 3, and 3 to 1. D, donor; R, recipient

Paired-kidney exchange

When available donors are incompatible with their intended recipients due to ABO or HLA antibodies, many transplant centers participate in kidney live-donor paired-exchange programs [18–20]. In a conventional PKE donation (two-way exchange), two donor–recipient pairs surmount each other's incompatibility problem by simply exchanging donors (Figure 1.4). To ensure that both recipients receive their grafts, the two transplantations are arranged simultaneously. The probability of finding a suitable donor–recipient pair for an exchange is greatly influenced by the pool size. Even in a successful large national PKE program, only around 50% of incompatible pairs usually find a match and undergo a transplant—primarily due to the blood-group imbalance in the pool of incompatible pairs [21]. There is a predominance of group A donors and group O recipients. National matching programs would make the likelihood of finding pairs greater and would likely expand this type of organ transplantation.

PKEs have been performed in the USA for nearly a decade, as either single-center or, increasingly, multiregional programs. A recent report showed that only 334 paired donations had been carried out in the USA since 2000 [22]. Legal and logistical barriers have been regarded as some of the major reasons for this poor success. Mutiregional data-sharing has substantially impacted PKE transplants [23]. There are now a number of regional PKE programs within the United Network for Organ Sharing (UNOS), such as the New England Program for Kidney Exchange (NEPKE), with 14 transplant centers in region 2, and the Alliance for Paired Donation, a 22-state coalition of 65 transplant programs. We believe a centralized national PKE program would give the greatest potential for matching incompatible donors. Such national schemes are currently operating in the Netherlands and the UK. The Dutch have reported numerous challenges and barriers in their exchange program, and a flexible organization was key to creating alternative solutions [20]. The rate of kidney transplantation can be increased by an average of 7–15% with a PKE program [24]. A recent study by the Dutch program suggested that the optimal chain length for living-kidney donation is three [25]. In the UK experience, the use of altruistic, nondirected donors to start a

chain of transplants may offer the greatest potential to increase the number of successful paired-kidney-donation transplants [26].

Altruistic donors

The success of living unrelated kidney transplantation has influenced transplant physicians to sanction the requests of individuals who wish to be anonymous donors; that is, "nondirected or altruistic donors" [27]. The motives of the nondirected donor should be established with care in order to avoid a prospective donor's intention of remedying a psychological disorder via donation. In general, these kidneys are allocated according to the waiting list for deceased-kidney donors [27]. Some centers advocate the allocation of such organs into a PKE program, since this can result in a domino effect and facilitate multiple transplants [23,28]. Directed donation to a stranger—whereby donors choose to give to a specific person with whom they have no prior emotional connection—is generally not supported, primarily because of fears of commercial incentive or psychological coercion [29].

Organ commercialism, which targets vulnerable populations (such as illiterate and impoverished persons, undocumented immigrants, prisoners, and political or economic refugees) in resource-poor countries, has been condemned by international bodies such as the World Health Organization (WHO) for decades. In recent years, as a consequence of the increasing ease of Internet communication and the willingness of patients in rich countries to travel to purchase organs, organ trafficking and transplant tourism have grown into global problems. For example, as of 2006, foreigners received two-thirds of the 2000 kidney transplants performed annually in Pakistan [30].

An international transplantation summit was held in Istanbul in 2008, which resulted in the "Declaration of Istanbul on Organ Trafficking and Transplant Tourism" [30–33]. This proclaims that the poor who sell their organs are being exploited, whether by richer people within their own country or by transplant tourists from abroad. Moreover, transplant tourists risk physical harm by unregulated and illegal transplantation. Participants in the Istanbul summit concluded that transplant commercialism, transplant tourism, and organ trafficking should be prohibited. They also urged their fellow transplant professionals, individually and through their organizations, to put an end to these unethical activities and foster safe, accountable practices that meet the needs of transplant recipients while protecting donors.

Evaluation process for the live donor

Living donation appears contrary to the most fundamental concept of the medical profession: "*primum non nocere*" ("first, do no harm"). It exposes a healthy individual to the combined risks of major surgery and life with a single kidney entirely for the benefit of another person. With that in mind,

LDK transplantation should only be undertaken if five essential conditions are met:

- The risk to the donor is low.
- The donor is fully informed of the risks and benefits as a donor
- The donor is medically and psychosocially suitable.
- The decision to donate is voluntary and entirely without coercion.
- The transplant has a good chance of providing a successful outcome for the recipient.

The Amsterdam consensus statement emphasizes that the purpose of the evaluation process is to ensure the overall health and well-being of the donor, minimizing unnecessary medical risk to both donor and recipient [34]. It should quantify any potential technical difficulties that might compromise the success of the nephrectomy and subsequent transplantation.

By general consensus, the optimal donor is an adult member of the immediate family of a patient with ESKD [29]. However, the use of emotionally related but genetically unrelated living donors has become increasingly common worldwide, and this practice is supported by different guidelines.

It is generally accepted that children (under the age of 18) should not donate. As can be seen in Table 1.4, the majority of donors in the USA are between 35 and 49 years old; nonetheless, the upper age limit has been advancing in recent years. There are no set guidelines for an upper age limit for donation, but most centers accept donors up to 70 years of age, after a thorough investigation for underlying kidney disease, latent cardiovascular disease, or malignancy.

A written informed consent is mandatory in most countries, with the understanding that consent can be withdrawn at any time. Moreover, the donor evaluation should ideally be undertaken by a physician who is not directly involved with the proposed transplantation or the recipient's care, in order to avoid any bias in the process. If the potential donor decides not to donate, the recipient is usually told that the donor is 'unsuitable'; detailed information should not be given, nor should untrue statements be

Table 1.4 Number of kidney donors by age in the USA. Data from [5].

	2009	2008	2007	2006	2005
All Ages	6,388	5,968	6,043	6,435	6,571
6–10 Years	0	0	0	0	0
11–17 Years	3	0	0	1	0
18–34 Years	1,937	1,849	1,872	2,034	2,078
35–49 Years	2,746	2,593	2,675	2,938	3,103
50–64 Years	1,595	1,437	1,415	1,390	1,332
65 +	107	89	81	71	58

made. Some controversial positions might arise when recipients are HIV positive and the potential live-related donor is not aware of the recipient's HIV status. The UK guidelines specify that the donor has the right to know the HIV status of the recipient in order to have a fully informed consent [35]. Others might argue that it is essential to inform the donor about the high-risk status of the recipient, but it is not necessary to give additional medical details about the recipient's condition.

The financial aspects of donation should be discussed, due to the important implications early after transplant. The future donor must be aware of any expenses involved with the surgery and postsurgical care, as well as the loss of income in the first few weeks after transplant, where activity is limited. The latter is minimized significantly by the use of a laparoscopic approach to harvesting the donor kidney. Moreover, congressional legislation in the USA has provided an important model to remove financial disincentives to being a live donor: federal employees are now afforded paid leave and coverage for travel expenses.

During the initial evaluation, the potential donor is assessed for any obvious medical or psychosocial contraindication to donation in order to avoid unnecessary further investigation. Some laboratory information is also collected during this first visit, including serum creatinine, blood count, urine dipstick, and ABO/HLA typing. The major contraindications for kidney donation are known diabetes, significant hypertension or proteinuria, a glomerular filtration rate (GFR) below the stated acceptable value for age, active infection, active malignancy, and recurrent kidney stones [36]. Serology for infectious diseases, chest x-ray (CXR), electrocardiogram (ECG), purified protein derivative (PPD) skin test for tuberculosis, and cancer screening exams appropriate for age are also performed. As a final step, renal imaging is done, typically with a computed tomography (CT) angiogram, in order to assess kidney size, the renal vessels, and the urinary tract. More details of the donor evaluation process can be found in [34] and [36].

Obesity in not considered a contraindication in either US or European guidelines, but it has been documented that a body mass index (BMI) over 30 significantly increases the perioperative complication rate, and some concerns exist about the long-term consequences of nephrectomy.

The evaluation for hypertension should include blood pressure (BP) measurements by an experienced provider on three separate occasions; verification of elevated levels should be undertaken with ambulatory BP monitoring as approximately 10–20% may be found to have normal BP [37,38]. If elevated BP is detected and the prospective donor is still under consideration, a CXR, ECG, echocardiogram, and ophthalmologic evaluation should be performed to look for secondary consequences of hypertension. In addition, a 24-hour urine collection for albumin excretion or a spot urine for albumin–creatinine ratio should be performed, along with a urinalysis and a formal GFR measurement. If donors with hypertension donate, they should be followed longitudinally by the transplant center to ensure optimal treatment and monitoring of complications. Overall, hypertensive donors are increasingly being used in transplant centers due to the limited availability of organs; however, more detailed information

about these donors and their long-term outcomes is needed before they can be generally accepted [38,39].

GFR tends to decrease with age, with an approximately 10 ml/minute drop per decade after age 40. In general, it seems prudent to require living donors to have a GFR at the average of the age-specific GFR [40]. In obese and elderly patients, GFR cannot be estimated accurately with the Cockroft–Gault or Modification of Diet in Renal Disease (MDRD) equations [40]. The majority of centers use a radioisotope exam to estimate the GFR (e.g. $^{51}Cr\ EDTA$) and assess this against the lower limit for the age of the donor, which can be seen in Table 1.5 and Figure 1.5 [36,41].

Table 1.5 Acceptable glomerular filtration rate (GFR) by donor age prior to donation. Data from [5].

Donor age (years)	Acceptable corrected GFR prior to donation (ml/min/1.73 m^2)
Up to 46	80
50	77
60	68
70	59
80	50

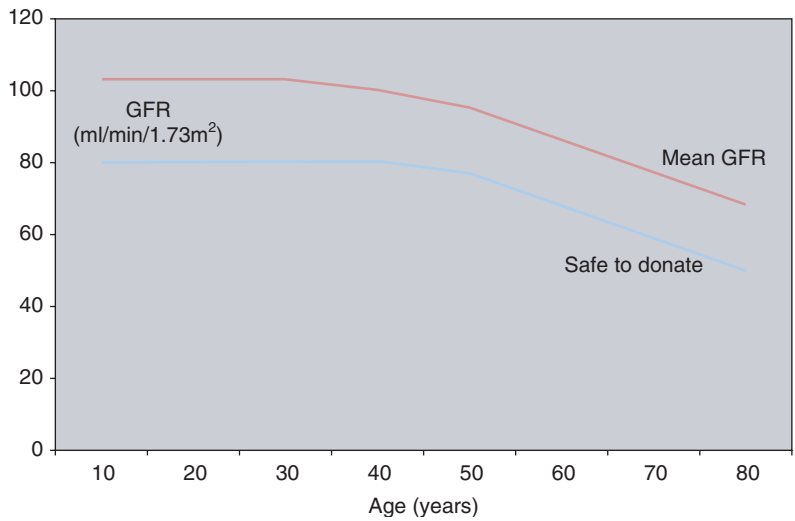

Figure 1.5 Graph of acceptable GFR by donor age prior to donation [36]. (Reproduced from http://www.renal.org/Libraries/Other_Guidlines/BTS_and_RA_Guideline_on_Living_Donor_Kidney_Transplantation_3rd_Edition_April_2011.sflb.ashx with permission from The British Transplantation Society and The Renal Association)

Short-term and long-term risks of kidney donation

The donor must be fully informed of the risks of surgery: donor nephrectomy is associated with a very low perioperative risk, with mortality of 0.03% being commonly reported [42]. It has been suggested that the risk can be compared with that of dying in a car accident during the next year, to enable potential donors to grasp the practical meaning of such an incidence rate. Laparoscopic nephrectomy now accounts for >50% of the donor nephrectomy procedures in the USA [43]. This technique has led to shorter hospital stays (2–4 days, compared with 3–7), less incisional discomfort, and an earlier return to work (12–21 days, compared with 30–60) than after open procedures [43–45]. Bleeding was the most common reason for reoperation after non-hand-assisted laparoscopic donation [45]. The most important perioperative risks due to donor nephrectomy include atelectasis, pneumothorax, pneumonia, urinary-tract infection (UTI), wound complications, and deep vein thrombosis with or without pulmonary embolism. In a cohort of 2509 living-donor nephrectomies, the risk of major morbidity for all donors was 4.9% (laparoscopic = 4.5%, open = 5.1%, p = 0.549) and the overall rate of any morbidity was 14.3% (laparoscopic = 10.3%, open = 15.7%, p = 0.001) [46].

The first study to attest the long-term safety of unilateral nephrectomy came from sixty-two World War II veterans who had undergone nephrectomy owing to trauma [47]. Mortality was not increased and autopsy results available in 20 cases did not show any evidence of glomerulosclerosis. More recent studies have confirmed no significant risk to the kidney donors up to 35 years after nephrectomy [42,48]. Decline in renal function parallels that of age-related healthy individuals with two kidneys. Urine albumin excretion, attributable to single-nephron hyperfiltration from reduced renal mass, may be elevated but is usually low-grade and not associated with higher risk for renal dysfunction.

The largest trial included 3698 kidney donors with a mean of 12 years of follow-up [48]. The population studied was very healthy, with no evidence of hypertension or proteinuria (<200 mg/day). There was no difference in the incidence of ESKD, hypertension, or renal dysfunction when compared to controls matched for age, sex, and race. There was also no survival difference when compared to controls from the general population. However, the time since donation was significantly associated with the development of albuminuria. The subgroup that was compared to controls represented mainly Caucasians (99%), with a predominance of females (60%). Extrapolation of the results to African Americans, Latinos, and South Asians, subgroups in whom chronic kidney disease tends to progress more rapidly, is not reasonable. One of the issues with using the general population as the comparative group is that kidney donors are a preselected group of patients with no significant medical comorbidities and excellent survival to start with, leading to a selection bias and possibly masking a potential deleterious effect of organ donation.

Nonetheless, the published evidence indicates that there is little long-term medical risk to a healthy donor after unilateral nephrectomy. However, the profile of the donor has recently changed to include those with isolated medical abnormalities such as hypertension, an increased BMI, dyslipidemia, and stone disease [19]. Further validation is necessary to ensure these donors do not see significant consequences from having a single kidney later in life.

Conclusion

Living-kidney-donor transplantation provides the best alternative for most patients with advanced chronic kidney disease. Due to the shortage of deceased kidney donors and the increased prevalence of ESKD, rates of living donation will continue to increase in the near future. In addition, innovative approaches that allow incompatible donor recipients to undergo transplantation are being developed, increasing the pool of potential organ recipients. Nonetheless, donor safety should always be kept in mind and we strongly advocate for the creation of national donor registries, which will allow close monitoring of the donors in the long term and ensure the preservation of our fundamental rule of "*primum non nocere*."

References

1 Merrill JP, Murray JE, Harrison JH, Guild WR. Successful homotransplantation of the human kidney between identical twins. *J Am Med Assoc* 1956;160(4):277–282.

2 Laupacis A, Keown P, Pus N, Krueger H, Ferguson B, Wong C, *et al*. A study of the quality of life and cost-utility of renal transplantation. *Kidney Int* 1996;50(1):235–242.

3 Evans RW, Manninen DL, Garrison LP Jr,, Hart LG, Blagg CR, Gutman RA, *et al*. The quality of life of patients with end-stage renal disease. *N Engl J Med* 1985;312(9):553–559.

4 Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, *et al*. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999;341(23):1725–1730.

5 OPTN Organ Procurement and Transplantation Network Database. http://optn.transplant.hrsa.gov/data/ [accessed 04/01/2010]. 2010; US Department of Health and Human Services.

6 US Renal Data System. USRDS 2009 Annual Data Report: Atlas of End-Stage Renal Disease in the United States. http://www.usrds.org/2009/pres/SA_FC346_mortality_10_31_09.pdf [accessed 04/15/2010]. 2009; Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases.

7 Sheehy E, Conrad SL, Brigham LE, Luskin R, Weber P, Eakin M, *et al*. Estimating the number of potential organ donors in the United States. *N Engl J Med* 2003;349(7):667–674.

8 Price D. Living kidney donation in Europe: legal and ethical perspectives—the EUROTOLD Project. *Transplant International* 2008;7(S1):665–667.

9 Sarnak MJ, Levey AS. Cardiovascular disease and chronic renal disease: a new paradigm. *Am J Kidney Dis* 2000;35(4 Suppl 1):S117–S131.
10 Meier-Kriesche HU, Schold JD, Srinivas TR, Reed A, Kaplan B. Kidney transplantation halts cardiovascular disease progression in patients with end-stage renal disease. *Am J Transplant* 2004;4(10):1662–1668.
11 Glanton CW, Kao TC, Cruess D, Agodoa LY, Abbott KC. Impact of renal transplantation on survival in end-stage renal disease patients with elevated body mass index. *Kidney Int* 2003;63(2):647–653.
12 Meier-Kriesche HU, Kaplan B. Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: a paired donor kidney analysis. *Transplantation* 2002;74(10):1377–1381.
13 Meier-Kriesche HU, Port FK, Ojo AO, Rudich SM, Hanson JA, Cibrik DM, *et al*. Effect of waiting time on renal transplant outcome. *Kidney Int* 2000;58(3):1311–1317.
14 Terasaki PI, Cecka JM, Gjertson DW, Takemoto S. High survival rates of kidney transplants from spousal and living unrelated donors. *N Engl J Med* 1995;333(6):333–336.
15 Mange KC, Joffe MM, Feldman HI. Effect of the use or nonuse of long-term dialysis on the subsequent survival of renal transplants from living donors. *N Engl J Med* 2001;344(10):726–731.
16 Fehrman-Ekholm I, Brink B, Ericsson C, Elinder CG, Duner F, Lundgren G. Kidney donors don't regret: follow-up of 370 donors in Stockholm since 1964. *Transplantation* 2000;69(10):2067–2071.
17 Kawai T, Cosimi AB, Spitzer TR, Tolkoff-Rubin N, Suthanthiran M, Saidman SL, *et al*. HLA-mismatched renal transplantation without maintenance immunosuppression. *N Engl J Med.* 2008;358(4):353–361.
18 Montgomery RA, Zachary AA, Ratner LE, Segev DL, Hiller JM, Houp J, *et al*. Clinical results from transplanting incompatible live kidney donor/recipient pairs using kidney paired donation. *JAMA* 2005;294(13):1655–1663.
19 Davis CL, Delmonico FL. Living-donor kidney transplantation: a review of the current practices for the live donor. *J Am Soc Nephrol* 2005;16(7):2098–2110.
20 de Klerk M, Keizer KM, Claas FH, Witvliet M, Haase-Kromwijk BJ, Weimar W. The Dutch national living donor kidney exchange program. *Am J Transplant* 2005;5(9):2302–2305.
21 de Klerk M, Witvliet MD, Haase-Kromwijk BJ, Claas FH, Weimar W. A highly efficient living donor kidney exchange program for both blood type and crossmatch incompatible donor-recipient combinations. *Transplantation* 2006;82(12):1616–1620.
22 Hanto RL, Reitsma W, Delmonico FL. The development of a successful multiregional kidney paired donation program. *Transplantation* 2008;86(12):1744–1748.
23 Ferrari P, de Klerk M. Paired kidney donations to expand the living donor pool. *J Nephrol* 2009;22(6):699–707.
24 de Klerk M, Weimar W. Ingredients for a successful living donor kidney exchange program. *Transplantation* 2008;86(4):511–512.
25 De Klerk M, Van Der Deijl WM, Witvliet MD, Haase-Kromwijk BJ, Claas FH, Weimar W. The optimal chain length for kidney paired exchanges: an analysis of the Dutch program. *Transpl Int* 2010;23(11):1120–1125.
26 Johnson RJ, Allen JE, Fuggle SV, Bradley JA, Rudge C. Early experience of paired living kidney donation in the United kingdom. *Transplantation* 2008;86(12):1672–1677.
27 Matas AJ, Garvey CA, Jacobs CL, Kahn JP. Nondirected donation of kidneys from living donors. *N Engl J Med* 2000;343(6):433–436.

28 Rees MA, Kopke JE, Pelletier RP, Segev DL, Rutter ME, Fabrega AJ, *et al*. A nonsimultaneous, extended, altruistic-donor chain. *N Engl J Med* 2009; 360(11):1096–1101.
29 Kasiske BL, Ravenscraft M, Ramos EL, Gaston RS, Bia MJ, Danovitch GM; Ad Hoc Clinical Practice Guidelines Subcommittee of the Patient Care and Education Committee of the American Society of Transplant Physicians. *The evaluation of living renal transplant donors: clinical practice guidelines. J Am Soc Nephrol* 1996;7(11):2288–2313.
30 The Declaration of Istanbul on Organ Trafficking and Transplant Tourism. *Clin J Am Soc Nephrol* 2008;3(5):1227–1231.
31 Reed AI, Merion RM, Roberts JP, Klintmalm GB, Abecassis MM, Olthoff KM, *et al*. The Declaration of Istanbul: review and commentary by the American Society of Transplant Surgeons Ethics Committee and Executive Committee. *Am J Transplant* 2009;9(11):2466–2469.
32 The Declaration of Istanbul on organ trafficking and transplant tourism. *Kidney Int* 2008;74(7):854–859.
33 The Declaration of Istanbul on Organ Trafficking and Transplant Tourism. Istanbul Summit April 30–May 2, 2008. Nephrol Dial Transplant 2008;23(11): 3375–3380.
34 Delmonico F. A report of the Amsterdam Forum on the Care of the Live Kidney Donor: data and medical guidelines. *Transplantation* 2005;79(6 Suppl):S53–S66.
35 Bright PD, Nutt J. The ethics surrounding HIV, kidney donation and patient confidentiality. *J Med Ethics* 2009;35(4):270–271.
36 United Kingdom Guidelines for Living Donor Kidney Transplantation. 2011. Available from http://www.bts.org.uk/transplantation/standards-and-guidelines/.
37 Textor SC, Taler SJ, Larson TS, Prieto M, Griffin M, Gloor J, *et al*. Blood pressure evaluation among older living kidney donors. *J Am Soc Nephrol* 2003;14(8):2159–2167.
38 Textor SC, Taler SJ, Driscoll N, Larson TS, Gloor J, Griffin M, *et al*. Blood pressure and renal function after kidney donation from hypertensive living donors. *Transplantation* 2004;78(2):276–282.
39 Torres VE, Offord KP, Anderson CF, Velosa JA, Frohnert PP, Donadio JV Jr,, *et al*. Blood pressure determinants in living-related renal allograft donors and their recipients. *Kidney Int* 1987;31(6):1383–1390.
40 Rule AD, Gussak HM, Pond GR, Bergstralh EJ, Stegall MD, Cosio FG, *et al*. Measured and estimated GFR in healthy potential kidney donors. *Am J Kidney Dis* 2004;43(1):112–119.
41 Bia MJ, Ramos EL, Danovitch GM, Gaston RS, Harmon WE, Leichtman AB, *et al*. Evaluation of living renal donors. *The current practice of US transplant centers. Transplantation* 1995;60(4):322–327.
42 Najarian JS, Chavers BM, McHugh LE, Matas AJ. 20 years or more of follow-up of living kidney donors. *Lancet* 1992;340(8823):807–810.
43 Matas AJ, Bartlett ST, Leichtman AB, Delmonico FL. Morbidity and mortality after living kidney donation, 1999–2001: survey of United States transplant centers. *Am J Transplant* 2003;3(7):830–834.
44 Schweitzer EJ, Wilson J, Jacobs S, Machan CH, Philosophe B, Farney A, *et al*. Increased rates of donation with laparoscopic donor nephrectomy. *Ann Surg* 2000;232(3):392–400.
45 Jacobs SC, Cho E, Foster C, Liao P, Bartlett ST. Laparoscopic donor nephrectomy: the University of Maryland 6-year experience. *J Urol* 2004;171(1):47–51.

46 Hadjianastassiou VG, Johnson RJ, Rudge CJ, Mamode N. 2509 living donor nephrectomies, morbidity and mortality, including the UK introduction of laparoscopic donor surgery. *Am J Transplant* 2007;7(11):2532–2537.
47 Narkun-Burgess DM, Nolan CR, Norman JE, Page WF, Miller PL, Meyer TW. Forty-five year follow-up after uninephrectomy. *Kidney Int* 1993;43(5): 1110–1115.
48 Ibrahim HN, Foley R, Tan L, Rogers T, Bailey RF, Guo H, *et al*. Long-term consequences of kidney donation. *N Engl J Med* 2009;360(5):459–469.