

Ethical Issues in Living Donor Kidney Transplantation

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The ethical issues of living donor kidney transplantation, which is the treatment of choice for patients with end-stage renal failure, are the focus of intense debate. Some of those issues are related to the safety of the operation for the donor, and others are related to the motivation of the donor, the approach to and evaluation of the donor, donation by strangers, the commercialization of donation, surrogate consent for donation, and the acceptance of minors as donors. The lack of clear consensus regarding these issues results in differences in practice, not only among countries but also among transplant centers. We believe that after an open debate, agreement on certain generally accepted principles can be achieved. Such an agreement would protect potential donors and recipients and would ensure the future of living donor kidney transplantation.

Key words: *Renal failure, Kidney transplantation, Living donor, Ethical issues, Paid donation*

Living donor kidney transplantation is an amazing act of altruism that forever affects the life of the donor and that of the recipient and his or her family. Some of the greatest triumphs of modern surgery are associated with living donor transplantation. Those achievements result from a high degree of inspired and extremely diligent work by multidisciplinary medical teams and from the courage and determination of the patients and their families.

Living donor kidney transplantation is the treatment of choice for patients with end-stage renal failure for the following reasons: a) the transplant is

performed when the donor and the recipient are in optimum medical condition and at a time that is convenient for them and for their families, b) recipients of living donor kidney grafts enjoy greater long-term graft survival and a better quality of life than do recipients of cadaveric kidney grafts [1, 2, 3], c) living donor kidney transplantation reduces the cost of health care for every patient with end-stage renal failure, because the cost of dialysis (which is £60,000/patient/y in the United Kingdom (UK) at the time of this writing) is supplanted by the cost of living donor kidney transplantation (which is £25,000/patient, including the cost of immunosuppressive medications, which is £3000/patient/y), and d) it reduces the number of patients on the wait list for a cadaveric kidney and therefore increases the likelihood that patients with no potential living donor can undergo transplantation. This is particularly important because the gap between the number of cadaveric donors and the number of patients on the waiting list is increasing in the UK. That growing discrepancy can be explained partly by the development of strong national campaigns for safe driving, a significant improvement in the safety features of vehicles (eg, airbags), and more stringent monitoring of motorists by the police (which has caused a significant reduction in traffic accidents), as well as the promotion of more healthy lifestyles with emphasis on exercise and improved dietary habits (and the subsequent reduction in the incidence of stroke). Data from the UK Transplant (the national regulatory authority for organ donation and transplantation) showed that between 1994 and 2003, there was an increase of 60.1% in the number of patients on the waiting list for a cadaveric kidney transplant and a 16.7% decrease in the number of cadaveric donors [4]. In fact, an increasing number of patients worldwide are maintained on dialysis, but in most countries, the number of donors fails to meet the demand or is even decreasing, as has been the case in the United Kingdom.

Retrieving a kidney from a healthy individual and

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exposing that donor to the risks of surgery (however safe the procedure might be when performed by experienced clinicians and in modern transplant centers) and to the potential long-term effects on health and quality of life for the benefit of another person poses several ethical questions that have engendered much medical and public debate.

Ethical Issues

Safety

The first issue pertains to the safety of the surgical removal of a kidney from a healthy individual, the long-term consequences of living with 1 kidney, and the effect of such a procedure on the donor's quality of life. The mortality rate of donors who undergo nephrectomy has been calculated to be 0.03% [5], and the life expectancy of a kidney donor is similar to that of individuals in the general population worldwide [6, 7]. Many surveys have reported that living kidney donors have an excellent postsurgical quality of life [8-12], and a meta-analysis of the minority who experienced negative feelings after donation showed that the dissatisfied donors had provided a kidney to a recipient who died within 1 year after the procedure. Although animal studies have demonstrated that glomerular hyperfiltration in the remaining kidney could eventually compromise renal function, it has been proven by several studies with a follow-up of more than 20 years that the remaining kidney did not exhibit any functional abnormality [13, 14] apart from a slight but insignificant increase in the degree of proteinuria [15]. The longest follow-up of individuals with 1 kidney was the 45-year monitoring of 62 World War II veterans who had undergone uninephrectomy after renal trauma, yet their survival rate was similar to that of other veterans from that war [16].

There are 3 types of living donor nephrectomy: the classic open nephrectomy, in which a wide flank incision is used; the laparoscopic nephrectomy, which is a type of key-hole surgery; and the mini-open nephrectomy, which involves a small loin incision of 8 ± 1 cm that is made anterior to the eleventh rib without rib resection and with the use of laparoscopic instruments [17]. The classic open operation may serve as a disincentive for the donor because it results in increased surgical pain, a longer hospital stay, a poor cosmetic result, and an extended period of convalescence. With the introduction of minimally invasive techniques, postsurgical morbidity in kidney donors has decreased, those patients demonstrate an early return to normal daily activities (as well as work), and the cosmetic result is excellent.

When laparoscopic nephrectomy was introduced as a surgical option, it was considered harmful

because it involves a longer warm-ischemia time (the period from the clamping of the renal vessels until the perfusion of the retrieved kidney with cold preservation solution) than does to the open operation, but with the advent of modern devices (eg, EndoCatch, US Surgical Corp, Norwalk, Conn, USA), this period has been shortened to a duration comparable to that in open nephrectomy [18]. The results of a survey by Pradel and colleagues showed that although the introduction of laparoscopic nephrectomy positively influenced potential recipients, probably because they anticipated minimal complications for their kidney donor, it had less impact on potential donors' decision to donate [19]. However, patients who undergo laparoscopic donor nephrectomy experience an increased incidence of ureteric complications, and the pneumoperitoneum decreases renal cortical blood flow and urine output [20, 21]. Mini-open nephrectomy offers the advantages of laparoscopic nephrectomy and reduces both the warm-ischemia and the duration of surgery, so that this procedure is even safer than laparoscopic surgery for the potential donor [17]. Life insurance companies in the United States have acknowledged the facts cited above. According to Spital, 94% of such companies did not consider a healthy donor to be at increased risk of morbidity or mortality after renal donation, and only 2% increased the insurance premium for such a donor [22].

Donor's motivation

Another important ethical issue is the motivation of the donor. In several recent surveys [23, 24], various categories of motives have been identified in living donors. Many donors have a very compelling desire to help that might be considered a natural response to another person's suffering. Some donors are motivated by a sense of moral duty; that is, a perception that donation is an obligation. Most donors derive a tremendous degree of satisfaction and an increase in self-esteem from performing good deeds. Also, some donors (especially siblings) identify with the recipient's situation and are sure of reciprocity if the roles of donor and recipient were reversed. A spouse may be motivated by anticipated benefit from their companion's improved health and an improvement in shared quality of life. Parents who donate may have those feelings as well as a sense of moral duty. Rare motives for kidney donation include religious beliefs or a feeling of guilt from a past relationship. A small percentage of donors feel coerced to donate, especially by other family members, and may fear that the family equilibrium would be disturbed if they refused.

Donor's feelings about donation

The decision to donate is a psychologically complicated one. For example, a potential donor who has an emotional relationship with the recipient is informed that dialysis is an option and that kidney transplantation is not a life-saving procedure; still, the donor feels that transplantation is the only option for the recipient [24]. A Scandinavian survey showed that men regard donation as an extraordinary gift but women regard it as an extension of family obligations [23]. Many people think that the decision to donate is spontaneous, that donors do not usually experience negative consequences regarding family relationships, and that conflicts between the donor and his or her family members are rare [25]. However, to preserve sensitive family relationships, the transplant team should obtain the widest possible family consensus regarding the donor's decision to donate, thus minimizing the possibility of future conflict. Various surveys have revealed that most donors do not regret their decision to donate a kidney [26, 27] and would even encourage others to become a donor [12]. Other surveys have shown that although many parents immediately decide to donate a kidney to their child, some fathers experience ambivalence about that donation [28]. In the same study, it was demonstrated that for siblings, the decision to donate is more complex because the families of both siblings may be involved and interfere. Thus in such a case there is a possibility of conflict between relatives and in-laws.

Recipient's feelings about donation

Recipients have been shown to experience greater feelings of guilt than do donors, especially if the donor and recipient have a close relationship [29]. One study showed that adolescent recipients of parental grafts experienced strong feelings of obligation and indebtedness to the donor, which led to psychologic distress and social as well as familial alienation, probably because of the enhancement of typical parent-adolescent conflicts fueled by the transplant procedure [28]. However, other studies [30] did not demonstrate a negative impact on family relations in parent-to-child donations. Recipients are sometimes reluctant to accept the offer of a living donor kidney when it is offered to them. In 1 study, more than half of the subjects who were undergoing dialysis declined the offer of a living donor kidney because of concerns about the donor's health and the fear that the procedure would compromise their relationship with the donor [31].

Donor consent and evaluation

Before an individual is accepted as a potential kidney

donor, every effort must be made to ensure that his or her offer is genuine and voluntary. The person who consents to be a living donor should be "competent, willing to donate, free from coercion, medically and psychosocially suitable, [and] fully informed of the risks, benefits and alternative treatment available to the recipient [32]." The most important elements of securing informed consent are: ensuring the participant's understanding of the procedure and its implications and sequelae, confirming the participant's medical and psychologic suitability, educating the donor, ensuring the absence of coercion and the presence of free choice, and documenting informed consent.

Potential donors have the right to receive and understand all necessary information regarding organ transplantation, the potential risks and benefits for both donor and recipient, the expected outcome of the procedure, and the potential results of alternative treatments that could be offered to the recipient. The source of such information is essential and certainly should not be provided, for example, in a brochure or by the recipients' physician [23]. Transplant centers seem to be the potential donor's only source of information, because those facilities possess the scientific information necessary for an informed decision. However, a transplant center may have several reasons for facilitating organ donation. Transplants are a source of income, prestige, and funding for those institutions (which in their mission statement also may cite the strong desire to help the recipient). Donors should be informed about the negative results that they might experience after kidney transplantation. This might cause concern, but only a thoroughly informed donor can make a truly voluntary decision [33]. For those reasons, independent donor counselors with experience in issues related to living donor transplantation and medical ethics are required.

Some authors [1] have suggested that the first approach to a potential donor should come from the recipient and not from the latter's physician or surgeon, although either clinician could facilitate that process. Some studies have shown that the public may have unrealistic fears about transplantation that may act as a disincentive to donate [34, 35], and for that reason, more education about living donor kidney transplantation is needed. The best way of assessing whether a potential donor has been adequately informed is to note if he or she is surprised by anything that happens after consent is given [32].

All potential donors should be screened for

psychologic and emotional stability and must be warned about the psychosocial impairment that might occur during the postoperative period [36]. Potential donors in whom psychosis or substance abuse is identified should not be considered candidates for donation. Social evaluation of the potential donor is also necessary, because financial hardship and marital problems that indicate social instability can cause problems such as the exacerbation of a possible depressive disorder after kidney donation. A trained psychologist or social worker should perform the psychosocial evaluation of the potential donor.

The argument that potential donors require extensive information and time for reflection before deciding to donate is, according to some studies, a myth [37]. A quick decision to donate is valid (despite the fact that the donor might not be fully informed about the procedure and its effects), because rapid offers of organ donation made by close relatives of the recipient are often genuine and ethically acceptable [38]. However, adequate information should always be provided to the potential donor, and the donor's comprehension of his or her role in organ transplantation should be established. For example, it is crucial that a parent who could donate a kidney to his child be made aware of the option for donation. In cases in which the potential donor and recipient are close and emotionally connected, rapid or instant decision making should not invalidate consent. The donor's health should not under any circumstances be damaged for the sake of the recipient, even if the donor is prepared to accept that risk. For that reason, an offer by a prisoner to donate his sole kidney to his daughter after having donated a kidney to her a few years earlier was declined [39].

Potential donors may feel that they are obligated to donate to an emotionally related recipient and are thus denied true freedom of choice. How, it might be asked, could anyone deny donation when the life of a close relative is at stake? Moral and emotional commitments are not constraints of freedom but are instead a part of everyday life [40]. Yet how could anyone who refuses donation to a relative later face his or her family members? For that reason, an independent and experienced psychologist should confirm that the potential donor is free from coercion and external pressure. A mandatory "donor's advocate" should participate in the donation process to ensure the extensive discussion of all possible complications for the donor and the recipient (including death) that can result from the transplantation process. The donor should also have a specified length of time to review his or her decision to donate as well as the liberty to withdraw at any point during the evalua-

tion process. Some experts [41] believe that a reluctant donor should be provided with a medical alibi to justify his or her hesitation to the family. However, the general belief is that physicians should always be truthful and direct with their patients and must avoid lying or falsifying medical documents, both of which can result in catastrophic consequences.

Autonomy of the donor and the transplant team

Popular opinion dictates that it is the donor's sole right to donate an organ and that this decision should rest only with him or her [42]. Yet for physicians, the prevailing principle according to the Hippocratic Oath is to "do no harm." Does a surgeon have an obligation to remove a kidney on request? In liberal and democratic societies, everyone has the right to participate in dangerous activities (eg, extreme sports, body piercing, etc) according to personal choice, as long as those activities are not illegal or harmful to others, but the transplant procedure involves an "accomplice": the transplant surgeon. The rejection of a potential donor by the transplant surgeon may seem to be a paternalistic act, but the physicians of the potential recipient are also responsible for the potential donor's welfare yet must act in the best interest of their patient. Despite low rates of morbidity and mortality in organ donors, the transplant surgeon always risks causing harm to a healthy person. It is unethical for physicians to conduct harmful interventions and create medical problems deliberately, such as in the aforementioned example of the father-prisoner who wanted to donate his sole kidney to his daughter [39]. If the transplant physician feels unable to accept a potential donor, he or she should inform that donor of the reasons for rejection and offer a referral for a second opinion. A transplant surgeon may refuse to accept a donor who exhibits any of the following characteristics: a borderline medical problem (eg, borderline hypertension, which may be exacerbated after donation), advanced age, or the potential for complications during surgery.

Many donors are rejected because of advanced age, although one may wonder whether physical or biological age is important. Donors may argue that it is up to them to decide whether to undertake the risk of transplantation. What if an older mother wants to donate a kidney to her child whose health is deteriorating despite treatment with dialysis, even though that donation is considered ill-advised for the potential donor by the transplant center staff [43]? Should the determination of donor acceptability in such cases rest with the transplant center alone?

There are great variations in the exclusion criteria used by various transplant centers. For example, in a

survey of US transplant centers [6], potential donors with history of renal stones, microhematuria, alcohol abuse, or heroin or cocaine abuse were accepted by 56%, 56%, 89%, and 66% of those centers, respectively. Proteinuria, moderate obesity, heavy cigarette smoking, and type 2 diabetes were exclusion criteria for organ donation in 58%, 16%, 16%, and 12% of those centers, respectively [6]. To achieve consensus regarding the aforementioned criteria and because of the differences in exclusion criteria, more research about the outcome of organ donation from individuals with increased morbidity is required.

It has been suggested that in organ donors, an age of 55 years or older negatively affects 1-year and 5-year kidney graft survival rates [44, 45]. Others researchers have not found a difference in graft survival rates according to the age of the donor [46]. Grafts from older donors may display tissue inflammation at the time of procurement, which may increase immune recognition [47]. Age-related changes in the kidney involve the number and size of glomeruli in the nephron, a progressive decrease in the glomerular filtration rate, and an increase in immunogenicity [47]. However, some experts suggest that the physical age of the potential donor is unimportant and that the biological age of the donor should be the criterion for performing transplantation because despite the advanced physical age of an individual, his or her biological status and endurance may be comparable to that of younger individuals.

There is also debate about the length of time that a patient with renal failure should undergo dialysis. Studies have proven that a prolonged duration of treatment with dialysis has a negative effect on both graft survival [48] and recipient survival [49], probably because of the established association of end-stage renal disease with an increase in comorbid conditions and the rate of acute rejection caused by various immunologic mechanisms [50, 51]. Researchers also have found that preemptive transplantation—that is, transplantation before any treatment with dialysis—is associated with better graft survival than is transplantation performed after the initiation of dialysis [52-54]. Although in an initial study, a brief duration of dialysis (ie, < 6 months) worsened graft survival but not patient survival [52], a more recent study demonstrated that the worsening of the graft outcome became significant only after 6 months of dialysis and that the recipient survival was significantly worse after 1 year of dialysis [55]. These facts support the theory that we should allow the patient who is treated with dialysis for end-stage renal disease only a limited time to consider the advantages and disadvantages of such treatment and the probable posttransplant quality of

life, so that he or she can better appreciate life after transplantation.

Living unrelated donation

It has been well established that kidney grafts from living unrelated but emotionally related donors such as spouses, partners, or friends have better long-term survival than do grafts from cadaveric donors [56-58]. In the United States in 1987, spouses accounted for 2% of living kidney donors, yet by 1997 they accounted for almost 10% [42]. In a 1996 survey in the United States, 90% of transplant centers accepted emotionally related donors, 60% encouraged emotionally related donation, 40% of them preferred a spouse, and only 21% accepted a friend as a donor, thus demonstrating a marked change in attitudes since 1989 [59].

Advocates of spousal donation from the United States [59, 60], Japan [61], and Switzerland [62] have reported improved family psychodynamics, including a strengthening of the marital bond, restoration of the functional role of husband and wife, an improved sexual relationship, and emotional bonding with children. However, in certain cultures in which the man is the dominant figure, female spouses may be forced to donate. That is why spousal donation remains illegal in France [63] and is a complex procedure in the United Kingdom [64]. In the United Kingdom, the Unrelated Live Transplant Regulatory Authority (ULTRA) assesses the ethical and moral issues in proposed transplants between genetically unrelated individuals and requires both the potential donor and the recipient to write a personal statement about their emotional relationship as part of the procedure. There are propositions for the abolition of that requirement [65] because spousal donation is becoming acceptable via a simplified method in which the physician takes responsibility for the emotional relationship between donor and recipient. In the United States, a declaration that has been signed by both the donor and the recipient, who state therein that they are spouses or partners, is a requirement. On the other hand, surgeons against spousal donation suggest that because 30% to 40% of marriages end in divorce (as in some Scandinavian countries), an enduring, loving relationship cannot be guaranteed as a motive for such donation [66]. Friends have been reluctantly accepted as potential donors, and that practice has never been restricted, even though a friend might feel less pressure to donate than would a family member.

Donation by strangers

In the past, most transplant centers have disapproved of living donation between strangers (ie, nondirected donation) because of the donor's motivation for and

commitment to donation and his or her psychologic stability and understanding of the potential risks [67]. However, in recent surveys in the United States, there has been strong medical and public support for the acceptance of strangers as donors. Studies have found no regrets or psychologic implications in donors after nondirected donation [68]. Such donors may also benefit from an increase in self-esteem without feeling coerced by a sense of obligation.

Researchers have proposed that in nondirected donation, the donor and recipient should remain anonymous to each other and should meet only after the transplantation, if that is a mutual desire [69]. It has been suggested that true altruists do not need the name of those whom they help [70]. With respect to kidney donation, anonymity is often not respected, and there is a risk of future financial request from the donor. However, the donor might want to see the results of his or her good deed, and the recipient might want to express his or her gratitude to the donor. It is worrisome that in the United States, Internet sites (eg, www.matchingdonors.com) have been developed on which potential donors and recipients can communicate and discuss rewards for organs. Through that networking, the entire process of donation could run amok with devastating effects on living donor kidney transplantation.

In 1996, a German professor of surgery and head of a transplant center, Jochem Hoyer, MD, voluntarily donated a kidney to an unknown recipient chosen from the Munich transplantation wait list. That act led to proposals in Germany for the creation of a registry for nondirected donors [71]. It seems unethical to allow potential donors to specify particular characteristics of the recipient (eg, age or race), although some surgeons [72] have suggested that if people were allowed to donate to someone with whom they felt an emotional connection, the number of donated kidneys would rise. There are also those who doubt that anyone would consider nondirected donation without receiving a substantial reward [73].

Commercialization of organ donation

Perhaps the hottest debate in living donor kidney transplantation today involves a potential financial reward for the donor. In the United Kingdom, an act of Parliament in 1990 made the sale of organs illegal and stipulated that proof of a relationship between the donor and recipient must be genetically established before transplantation. This act was produced after a General Medical Council inquiry into the case of the involvement of a British physician in transplants involving Turkish peasants [65]. In the United Kingdom, the law requires that renal transplantation

in which the donor and recipient are not blood-related relatives (including spouses) must be approved by the ULTRA, whose chairman is appointed by the Secretary of State for Health [74]. In the United States, the transplant team is responsible for determining and assessing the motives of the donor, and the sale of organs is illegal. However, the shortage of cadaveric organs has led to a worldwide black market for living donor organs in which patients who possess the necessary means can purchase a kidney for transplantation.

The purchase of organs is a heinous act (the deontological ethical approach), but we must consider ways in which to increase the live-donor pool (the utilitarian ethical approach). For example, in Bombay, India, the price of a woman's kidney is alleged to be US\$1000; in Manila, the Philippines, a man's kidney is worth US\$2000; and in urban Latin America, a kidney can be sold for more than US\$10,000, with additional payments to the brokers in all cases [75]. Although Americans are purchasing kidneys from strangers in China, Peru, and the Philippines, the current federal law does not prevent those patients from returning to the United States for posttransplantation care [76, 77]. Furthermore, there are also allegations that affluent patients from other countries have paid at least US\$200,000 to undergo transplantation in United States centers as part of a package deal that includes the compensation of unrelated donors and is prearranged outside the United States by international brokers [75].

Some of the arguments for or against the commercialization of organ donation are as follows:

(a) It is unethical to sell your body or your organs because the importance of life is paramount and every human being is special. Organs cannot be regarded as commodities for sale. For the same reasons that render prostitution and child trading unacceptable, the commerce in human organs cannot be endorsed. Some might argue that in a free society, people are entitled to do anything that they want to do, including selling their organs, as long as the liberty of fellow citizens is not restricted by that action.

(b) A poor donor may be compelled by his or her financial status to donate, thus making that action obligatory. However, such a donor may be choosing the best of bad options, because organ donation confers significantly less risk than does working under harsh and dangerous conditions and offers the opportunity to contribute to the well-being of the recipient. Although the recipient may be taking advantage of the donor's difficult economic situation, the donor's financial status will not improve if the donation is refused.

(c) Many paid donors are poor and uneducated and may be unable to understand the risks involved in organ donation. It could easily be argued that it is the physician's duty to explain the whole procedure as simply and clearly as possible and to answer every question raised by the potential donor.

(d) Wealthy individuals will eventually have access to organs, but those who are poor will not. However, because private health care does exist, the wealthy receive better medical care than do the poor.

(e) The sale of organs facilitates the exploitation of donors and recipients by unscrupulous middlemen and surgeons. However, the sale of organs for transplantation may be even more prevalent in an illegal and uncontrolled environment that generates inferior medical care. The financial exploitation of donors could be avoided if donations were supervised and controlled by a national agency that would allocate organs nationally according to the best match and clinical need criteria and would maintain the anonymity of the donor-recipient relationship [78]. In such a setting, the safety of the donor and the recipient would be safeguarded by better preoperative, intraoperative, and postoperative care [79]. However, such a policy applied on a larger scale could lead to differences in financial compensation among transplant centers or countries that would encourage "donation tourism" from poor to wealthy areas of the world [79]. Other researchers who propose a closely regulated and supervised market of organs claim that society should not regard physicians as less caring because they are paid [80]. Because the long-term cost of renal transplantation is less than that required for maintenance dialysis, government or medical insurance organizations would save money. It also has been proposed [42] that wealthier patients could make financial contributions to a general independent fund that would pay potential donors, thus reducing the cost to the government even more. The initial selection and screening of potential donors could be performed by an independent physician, after which the transplant center would have the right to reject that donor after consultation with a specialist in medical ethics. A paid donor would not be able to select a specific recipient. Others fear that rewarding donors could lead to an increase in the cost of transplantation, because those who might donate a kidney altruistically could ask for compensation [81].

(f) Another argument against commercial donation is that the poor are unable to manage money [42]; thus payment for organ donation would make no long-term difference in the donor's poverty level. The possibility of misuse of the money paid for donation, although difficult to predict, does not justify

overriding the donor's decision.

(g) Transplantation has always relied on the altruism of donors, and paid donation may lead to the disappearance of altruistic donation, because it is possible that eventually, all donors will request to be paid.

(h) Even if the sale of organs is regulated, there is always the fear that some people will grossly exaggerate the risk of that procedure and will perpetuate urban legends about organ theft.

(i) Some investigators claim that living donation involves a "highly artificial enforced altruism" in which only the donor is required to be altruistic and all other individuals involved in the procedure benefit (eg, the transplant team and transplant coordinator are paid, and the recipient greatly benefits) [80]. However, those involved professionally with the transplant procedure do not receive extra payment for every transplant that they perform.

(j) In a hypothetical scenario, an impoverished father has a daughter with leukemia, and if she experiences renal failure, he will donate his kidney to her. Some researchers [82] posit that it would be morally acceptable for this father to sell one of his kidneys to earn money to pay for his daughter's treatment. However, the counterargument states that in such cases, a well-organized National Health Service should be able to provide the necessary resources and financial assistance for those individuals.

(k) Other investigators [83] consider the fact that wealthy individuals are free to engage in dangerous sports for pleasure while the poor are denied a possibly lesser risk of selling a kidney (which may save the life of the recipient) to be a facet of a paternalistic society. It is true that if kidney sales are allowed, wealthier people will have access to medical care that is unavailable to the poorer populace, but this is a worldwide reality, and outlawing such sales will not correct social inequities [84].

Information about several types of commercial donation is already available, although some centers involved in that practice are reluctant to report their results. One study revealed a higher perioperative (6.2%) and 3-month mortality rate (12.3%) and an almost 12% lower 1-year survival rate (81.5%) in recipients who purchased a kidney in a Middle Eastern country and were monitored by a nephrologist after returning home than in patients who underwent a nonrelated renal transplantation in a Western country [85]. In another study, although the graft survival rate of the patients who purchased a kidney was similar to that in patients who underwent a living unrelated transplant performed in another Middle Eastern country, there was a higher incidence

of severe infections for the former group of patients, including human immunodeficiency virus and hepatitis B infection [86]. Another report on commercial transplantation showed a high rate of severe complications in Palestinian children with end-stage renal disease who underwent transplantation in Iraq [87]. In a more recent study of Tunisian patients who purchased a kidney in Iraq (mean cost, US\$10,000 per kidney), Egypt, or Pakistan, there was a very high short-term and (especially) long-term complication rate [88]. Although there is still a black market for the purchase of kidneys in India because dialysis is very expensive and cadaveric donations are very rare, a paid donation program [89] was suspended after commercial donation was made illegal. Before paid donation became illegal, however, the careful screening of donors (72% were rejected) resulted in a 2-year graft survival from related as well as unrelated donors. Potential donors who were rejected were compensated for their time, and the eventual donors were offered free 3-year medical care.

In Iran, a compensated, controlled, living unrelated donor transplantation program that was established in 1988 resulted in the elimination of the renal transplant waiting list in that country by 1999 [90]. In the current Iranian transplant program, the government (without involving any middle men or agencies) pays all hospital expenses for the donor and provides him or her with an award and health insurance. Such a program in Middle Eastern countries, where strong cultural barriers exist against cadaveric donation and long-term dialysis is either unavailable or is very limited, could reduce the more than 50,000 annual deaths caused by end-stage renal disease [91]. In a recent survey in Hungary, 63.3% of those interviewed, who were prior donors, were not in favor of selling or purchasing organs, but all stated that if they were to experience end-stage renal failure, they would buy a kidney if one were available [92]. Finally, there is great concern that no matter how well-regulated an organ market is, dishonest brokers will find a way to bypass the regulated system and will use other means to obtain the highest price for an organ from prospective buyers who will bid for the most medically appropriate match [93].

Donor rewards

Even if we reject the commercialization of kidney donation, the question of whether donors should receive any reward remains. Most people would agree that donors should at least not suffer from having donated an organ and should receive certain reasonable rewards. Researchers [19] have discovered that some recipients and potential recipients were

unwilling to accept a kidney if that act would impose a financial burden on the donor. Thus it seems reasonable that if a kidney donor were to experience later renal failure, he or she should be placed at the top of the waiting list for a cadaveric kidney and should receive medical insurance and reimbursement for working hours or wages lost as a result of renal disease [94]. It is generally accepted that this support should be provided by a government authority such as the National Health Service [33]. The United Kingdom has implemented a sophisticated method for calculating the loss of working hours or wages and compensating donors fairly [74].

In 2001, during the first session of the 107th US Congress, new legislation was considered for the promotion of organ donation in the United States. It included the presentation of commemorative medals to donors, the offer of tax credits, and the reimbursement of travel and other expenses incurred as a result of donation. In addition, a 30-day paid medical leave for all federal and some state employees who become donors was established. The American Society of Transplantation is encouraging US transplantation centers to provide paid medical leave for employees who become donors and risk the loss of wages or employment as a result [75]. The transplantation program at the University of Minnesota in the United States offers a small financial aid incentive that is intended to minimize donor expenses that result from having undergone the procedure [95]. The US state of Pennsylvania has proposed a plan that offers organ donors and their families the sum of US\$300 to be used for expenses such as food, housing, and transportation [96].

The idea of noncash rewards for donors might preserve the concept of altruism, however. The Red Cross for example, gives T-shirts, food, and beverages to those who donate blood but does not provide a cash equivalent. Life and liberty, which are the foundations of our society, are values that should not have a price. Thus being awarded a medal or a certificate by the state for a generous and altruistic action might be reward enough. The recognition of donors in an official ceremony that receives media attention may further promote donation. Providing free medical follow-up and health insurance is also a substantial reward for donors and expresses society's gratitude for such altruistic acts. Providing free medical follow-up is also necessary to identify possible long-term risks for the sake of future donors and to ensure the early diagnosis and treatment of any illnesses that develop in those who have provided a kidney for transplantation. In a study in France [97], two-thirds of the transplant centers performed annual lifetime

health screenings for kidney donors, but the remaining centers examined donors once or twice before referring them to their personal physician for annual examinations (blood pressure measurement, serum creatinine, and screening for proteinuria).

Surrogate consent

The statement of the Live Organ Donor Consensus Group in 2000 that the donor must be competent to provide consent for donation rejects the validity of surrogates' consent to organ retrieval from an incompetent adult, although such examples occur occasionally [98] and have even been allowed [99]. In 1998 in Ohio, a judge ruled that a kidney could be removed from a comatose patient and given to his brother. The patient's condition was irreversible, and he could still live with 1 kidney. In addition, there was evidence that he wanted to become an organ donor [100]. The family's making the decision to donate the kidney of a patient who lacks decision-making ability because he or she will probably not regain consciousness is obviously not to that patient's benefit. How is it then possible to justify such an action? When family members have proven that they are expressing the patient's will, his or her autonomy is respected. The adult comatose patient nevertheless has a history of having made life choices based on personal values and priorities that can help his or her family decide. From a legal perspective, surrogates (such as the donor's family members) who make the decision regarding organ donation must also consider the best interests of the patient's family as a whole [101].

A medical center ethics committee at the University of California, Los Angeles [99] has proposed the following principles for surrogate consent: (a) the family members must be able to prove that their decision is based on the patient's will, (b) surrogates should not benefit from the donation except from the satisfaction of the altruistic act, (c) the procedure should not affect the clinical course of the donor, (d) all parties involved in the transplant procedure and those involved in the donor's care must believe that the donation is ethical, and (e) the consent to donate should be evaluated by an independent multidisciplinary body, such as an ethics committee, on a case-by-case basis.

Surrogate consent should be limited to patients with the least possibility of recovery and those who will die after the withdrawal of life support. Such patients include those in a permanent vegetative state (PVS). A PVS is considered irreversible. It is associated with a median survival of approximately 2 to 5 years if the vegetative state lasts more than 1 month in patients with no injury, more than 3 months in

patients with a nontraumatic injury, and more than 12 months in patients with a traumatic injury [102]. Is it possible to determine whether a vegetative state is truly permanent? We can consider as an example the recent report of a person who recovered partially and began to respond to questions after 19 years in coma [103]. That is why the surrogate should base his or her decision on what the patient would have chosen regarding donation, if that patient had been competent. Some authors [103] suggest that permitting surrogates to donate the nonvital organs (such as the kidneys) of terminally ill patients may undermine the public trust of transplant programs and will refer public financial support to other patient groups (eg, patients with Alzheimer's disease). These experts suggest that a surrogate's consent for living organ donation should be permitted only if the patient is in a PVS.

Paired-exchange programs

Another possible method of increasing the living donor pool involves the paired-exchange program, which was suggested in 1986 [104]. In such a program, pairs of potential donors who cannot donate to their potential recipients (primarily because of blood group incompatibility or a positive cross-match) instead arrange to donate eventually to the other donor's recipient; thus if donor A cannot donate to recipient B and donor C cannot donate to recipient D, the transplants are possible when donor A provides a kidney to recipient D, and donor C provides a kidney to recipient B [105]. In addition, instead of occurring as a direct exchange between donor pairs, kidney donations could be made via an exchange donor pool. Such a program that was developed in Korea in 1991 resulted in a significant 7.3% increase in living donor transplants [106]. The reasons for participating in the paired-exchange process were ABO incompatibility (75.5%), a poor HLA match (13.6%), and a positive lymphocyte cross-match (10.9%). The United States has also offered "kidney swapping" [107], but in Europe, paired-exchange transplantations have been attempted only in Switzerland, Romania, and the Netherlands [108].

A consensus statement from the Live Organ Donor Consensus Group in 2000 [32] stated that the meeting of the donor-recipient pair should be arranged only if all parties so choose and at the transplant center's discretion. A survey [108] performed among potential pairs participating in an exchange program showed that donors and recipients preferred anonymity as opposed to emotional involvement with others who had similar health problems, thus avoiding psychologic pressure that might develop

after acquaintance. Others [105] have suggested that strict confidentiality should be maintained for each donor-recipient pair because frustration, anger, or resentment may develop between the 2 pairs (for example, if the outcome of 1 recipient is not as good as that of the other recipient). It has also been suggested that both procedures should be performed simultaneously to avoid the possibility that 1 donor would refuse after the other donor's nephrectomy had been performed. In pair-exchange programs, the psychological pressure on the donor may be greater than that on the recipient, because the donor is asked to give a kidney to a stranger rather than to a loved one. Nonetheless, potential donors can understand that their donation will indirectly benefit their loved ones. Another ethical aspect of such a program is the possibility of coercion to donate, because a reluctant donor cannot use an excuse such as ABO incompatibility to obviate donation. Thus, a meticulous psychological evaluation of the donor should be conducted to ensure the donor's volition of action. With the advances in immunosuppression and plasma exchange techniques, such programs may be unnecessary, because ABO- and HLA-crossmatch incompatible transplants can be performed.

Minor donors

Another important issue under debate is whether minors (children younger than 18 years old) should be allowed to donate. Most kidneys transplanted to children come from their parents. However, that is not always possible for medical or other reasons. Should minors be allowed to donate a kidney to a sibling? From whom is consent required, and who should determine the need for such a transplant? What should the minimum age for donation be? These important questions must be answered.

Serious concerns about child donors exist. A child may be unable to comprehend the risks and benefits of the procedure and thus cannot provide valid informed consent. Some children who feel coerced by parents to donate believe that they cannot refuse donation without risking the loss of parental love and support. Parents of a child who requires a kidney transplant and has a healthy sibling (a potential donor) may experience a conflict of interest [109]. Finally, there are limited risks (trauma, the development of a neoplasm or infection) to the remaining kidney of a child donor that can alter his or her future, degree of physical activity, or career choice in fields such as athletics, military service, etc [110]. The preadolescent and adolescent years are very important in the emotional, physical, and intellectual development of a minor; thus there should be adequate justification

for disrupting that period of life with an operation that is not medically required. Issues such as postoperative convalescence and the disruption of school, activities, play, etc, can adversely affect the daily life of a child at a sensitive age.

Some experts suggest that older and younger child donors must be considered separately [109]. They posit that formal operational thought is usually well established at about the age of 14 years and that adolescents are as competent as adults with regard to making decisions about their health. In 1994, the Council on Ethical and Judicial Affairs of the American Medical Association considered adolescents 14 years of age and older as being mature enough to make decisions about their medical care but cautioned that this capacity must be evaluated in each adolescent. Thus, several states in the United States grant such "mature minors" the right to consent to medical treatment intended for their benefit [109]. Before accepting an adolescent's consent, his or her competence should be evaluated by a skilled mental health professional after consultation with the parents, who also should agree to the donation. In addition, the child's competence should be confirmed by the courts, as the Council on Ethical and Judicial Affairs of the American Medical Association has recommended. Data from that Council suggest that parental influence on a child's decision making decreases as the child ages. In a previous study [111], most young donors 16 to 20 years of age appeared to be under no family pressure to donate, and 1 year after having donated a kidney, most did not regret their decision. The aforementioned Council also recommended that health professionals and the courts should confirm that the adolescent donor is acting voluntarily. According to Spital, "although court involvement seems reasonable, it may be that a determination of competency and voluntarism can be achieved less traumatically, more efficiently, and at least as accurately by qualified health professionals alone [109]."

Regarding the risks of nephrectomy in children, the results of a large study [112] showed that renal function is maintained for up to 50 years after unilateral nephrectomy in pediatric patients. Thus accepting only kidney donors older than 18 years may be too restrictive for some transplant centers. As Hamburger and Crosnier demonstrated, it is very difficult to set an age limit below which a potential donor is rejected, because the decision to donate should depend on psychological maturity rather than age [113]. As a result, some US states have begun to legally accept the consent of minors older than 14 years for organ and tissue donation. In Alabama, for

example, minors of that age can consent to bone marrow donation, and in Michigan (with court approval), they can serve as a kidney donor for an immediate family member [109].

However, it is very difficult to accept "immature" minors (those younger than 14 years) as kidney donors, because they are unable to make sound decisions regarding their own health and their choices are greatly influenced by their parents. However, this approach could be considered very restrictive, and some experts suggest that under rare circumstances, even young minors should be allowed to donate [109]. We must therefore acknowledge that legislation accepts an incompetent individual as a potential donor only if donation is in his or her best interest and he or she benefits from it. Similar psychologic benefits for young children have been used by courts as justification for approving donations by minors, and those benefits were documented in a 7-year-old donor [114]. Some of the benefits for kidney donation by young children include: (a) preventing the trauma caused by the death of a very close relative such as a sibling, (b) avoiding future guilt resulting from the refusal to donate, (c) increasing self-esteem from donation, and (d) maintaining the integrity of the family [109]. However, we can only speculate about the psychologic benefits reaped by children who donate a kidney. For that reason, the Council on Ethical and Judicial Affairs of the American Medical Association has proposed that organ donation from a potential "immature" minor donor should be permitted only if the child's parents and the courts agree that "donation could provide a clear benefit to the donor [115]." Other experts recommend that the potential minor donor be examined by a child psychiatrist or child psychologist and that a guardian be appointed to ensure the protection of the potential donor's interests [116]. That procedure would require the following stringent safeguards:

(a) the child donor is the only available organ source, (b) the transplant procedure has a very high possibility of success, (c) the recipient will benefit from the transplant, (d) the recipient is a close family member, (e) the potential donor will likely benefit from the procedure, (f) the risk of donation is extremely small, and (g) the child freely agrees to the procedure (this requires that the child donor be old enough to make that decision [ie, age > 7 years]) [109]. Although those safeguards do not prohibit kidney donation by young children, they greatly limit the number of minors who can be considered as potential donors.

Surveys of US transplant centers have demonstrated that although great controversy regarding the acceptable age for kidney donors exists, the

acceptance of children as living kidney donors is decreasing [109] (a result that contradicts the findings of another similar study [117]). In the more recent of those 2 studies [109], the centers that sometimes accepted minors as donors required consent from the potential donor's parents (88%), the potential minor donor (75%), a court (69%), and an appointed guardian (50%).

Conclusions

The many ethical issues regarding living donor kidney transplantation have been under intense debate among countries, transplant centers, and physicians. Cultural, socioeconomic, and demographic factors make those issues even more complicated. However, we believe that after an open and honest debate that includes all interested parties, an agreement on certain generally accepted principles can be established. Such an agreement would protect potential donors, recipients, and their families and would ensure the future of living donor kidney transplantation.

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