Is Living Kidney Donation Still Justifiable?

Because of the shortage of cadaver kidneys for renal transplantation, the use of living kidney donors has been common practice for many years. For the same reason, living donors have recently been used for liver and lung transplants. Most experience has been with living-related donor kidney donation, but even now at 30 years after the first procedure, there are still concerns as well as advantages to living-related transplantations.

The major advantages for using living-related kidney donors are that a readily available organ avoids an indefinite waiting period for a cadaveric kidney and that the long-term survival of the transplanted organ and the recipient are better with live donor kidneys than with cadaveric organs. Dialysis therapy is a counterargument to the first justification, although physicians and patients prefer transplantation because of the better quality of life for the recipient. Dialytic therapy is inadequate and patients feel much better after transplantation. Uremia causes muscle dysfunction and metabolic abnormalities and these are totally reversible after the acquisition of a functioning allograft. Allograft rejection is also less of a problem since the introduction of cyclosporine and other newer immunosuppressive agents.

The major disadvantages and concerns in using living-related kidney donors are short-term surgical complications such as death, prolonged hospitalization, prolonged morbidity and time off work; and long-term complications such as proteinuria, hypertension, and end-stage renal disease. Because of increasing concern about these short- and long-term complications, some transplant centers have stopped using living-related donors.\(^1\)

Short-term surgical complications in the donor may be as high as 17 percent overall, although only 2.5 percent are classified as serious.\(^2\) The reported frequency of mortality from nephrectomy is low\(^3,4\) but not all deaths may be reported. Currently, the reporting of any morbidity or mortality associated with renal donation is required by the United Network for Organ Sharing (UNOS).

Long-term follow-up of kidney donors has produced conflicting data about the status of donors in regard to focal glomerulosclerosis, proteinuria, and hypertension. These late sequelae of nephrectomy are of great concern to many authors.\(^5,6\) A 50 percent reduction of renal tissue due to agensis or nephrectomy is associated with proteinuria and hypertension after 10 or more years and is called a “risky situation in humans,”\(^7\) although we must use the example of renal agenesis with caution since the person’s remain-

ing kidney may have structural abnormalities as well. A 10- to 20-year follow-up at several transplant centers, however, shows proteinuria and hypertension in a significant number of related kidney donors.\(^8-10\)

Prospective donors with a predisposition to develop hypertension or with predonation hypertension are likely to have acceleration in the development of or aggravation of hypertension after kidney donation.\(^9\) Perhaps they should be rejected as donors. At least one transplant center, however, reports that baseline characteristics do not predict which kidney donors are at risk of developing hypertension.\(^11\)

Other reports, however, state that the frequency of new cases of donors with hypertension after kidney donation is no higher than that of the general population,\(^8,12-16\) although most donors develop proteinuria over time. Most transplant centers report significant proteinuria and some also report an increased frequency of hypertension years after kidney donation; nevertheless, glomerular filtration is well preserved.\(^17\) Therefore, the conclusion of many investigators is that the consequences of renal donation are minimal over a long period. A recent study of morbidity 20 years or more after uninephrectomy and a comparison of renal function, hypertension, and proteinuria in donors with their siblings concluded that renal transplant donors are not at increased risk for development of renal failure.\(^15\)

In view of all this accumulating data about the short- and long-term risks of kidney donation, is the use of living donors still justifiable? An editorial published in 1985 considered unilateral nephrectomy in living-related kidney donors to be “safe and beneficial.”\(^18\) In 1987, another editorial concluded that “donor nephrectomy is associated with significant peri-operative morbidity and a small risk of mortality,” but that most donors can expect stable renal function and normal blood pressure for many years.\(^10\) However, the editorial writer suggests that “high-risk” donors or subjects with high “normal” blood pressure be rejected as kidney donors except in situations of extreme recipient need. In 1990, yet another editorial questions whether living donation is still justifiable.\(^30\)

How much risk is a live donor allowed or obligated to undertake to provide a kidney to a close relative with end-stage renal disease? Should the potential donor refuse to give a spare kidney because of the short-term anesthetic and/or surgical complications albeit rare? Should the potential donor refuse to give a spare kidney because of the long-term complications of proteinuria, glomerulosclerosis, and hypertension? How far can we expect altruism on the part of the potential donor to determine whether the decision to donate is affirmative or negative? If one can save the life of another human being at no risk to
oneself, one is certainly morally bound to do so. If there is great risk to the rescuer, the latter is not obligated (but is allowed) to endanger his life to do so. To throw a drowning victim a life preserver is morally required, but to jump into the water as a rescuer who cannot swim would be foolhardy.

What if the risk to the rescuer—in this case a potential kidney donor—is very small? How does one define small risk? If a donor wishes to give a kidney in spite of the risk, is this a pious and altruistic act or an act of folly? If the risk is very remote, the potential donor is certainly morally bound to consider donating a spare kidney.

The data cited above concerning short- and long-term complications of kidney donation do not easily lend themselves to categorizing risk as remote, rare, inconsequential, not significant, or of no concern. Just as the scientific data are interpreted differently by various scientists and investigators, the risk may be viewed differently by various potential donors. Specific forms of conduct by transplant centers should be followed to minimize donor risk and assure maximal understanding of the transplant process. Fully informed consent requires that all potential and actual risks be presented to a potential donor before an affirmative decision can be requested. The transplant center’s responsibility is to give the possible donor all of the available data on the risks. Such a prospective donor should receive a complete medical evaluation by a physician not involved in the care of the recipient. The donor should be allowed to state that he/she does not really want to donate without any family member finding out. The transplant center must accept the decision of the potential donor. There must also be strict medical criteria for disallowing donation. At many transplant centers, the donor must step forward voluntarily and ask about donation. The transplant center is not allowed to seek out the relatives who might be possible candidates.

The shortage of donated cadaver organs should not be a reason for transplant centers or families to pressure a potential living donor to give a kidney. Nor is the offering of cash rewards to relatives or unrelated donors an ethically acceptable solution. Payment is a type of coerced altruism, undermines the consent process, encourages a black market of covert payments for organs, and raises a series of “slippery slope” questions.21 Other methods of increasing organ procurement from living donors as well as cadaver organ donations have been proposed, most of which are ethically or socially objectionable.22

The shortage of kidneys is unlike many other scarce medical resources such as ICU beds or dialysis machines. Society can build more ICUs and purchase more dialysis machines as needed. The supply of living donor or cadaver kidneys, however, remains less than the demand, no matter how successful efforts are in recruiting new donors. Voluntary choice and altruism must remain the prevailing ethic of public policy toward organ donations. The long-term risk to potential living-kidney donors must be clearly delineated and discussed with the prospective donor allowing for a freely voluntary and uncoerced decision based on facts rather than emotion. It is ethical to ask for a live donor to give a kidney for his close relative with end-stage renal failure. It is unethical to pressure or coerce a donor to do so. A soft approach of asking for kidney donation permits an informed potential donor to become educated about the risks and to respond appropriately to an appeal to altruism. In spite of the short- and long-term risks to the donor, living-related donor transplantation seems still acceptable under certain conditions and with certain guidelines followed by all transplant programs.

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Aerosol Therapy in Mechanically Ventilated Patients

Aerosol therapy is a common method to administer medications to intubated patients. As indicated in the review article by Manthous and Hall in this issue of *Chest* (see page 560), characterization of the techniques of this practice has a paucity of experimental support, and factors affecting distribution and efficacy are not well characterized. It is clear that many drugs are effective when delivered as aerosols in spontaneously breathing, intubated patients, and if there is a measurable physiologic effect, this end point can be reached in intubated patients as well. Theoretic optimal particle size and deposition data suggest that 3- to 5-μm-sized particles will reach the conducting airways and 0.8 to 3 μm will reach and be deposited at the lung parenchyma. Smaller particles may be exhaled without impacting and have no pharmacologic effect. Factors reducing distal delivery include removal of particles in the ventilator circuit, endotracheal tube, trachea, and large airways, as well as airway obstruction (mucus or bronchospasm). Quantification of the influence of these factors in the published literature is scarce.

Delivery of drugs directly to the lung increases the local effectiveness and reduces the systemic toxicity. This improved therapeutic index has been demonstrated for β-acting agents, corticosteroids, and anti-cholinergics. Surfactants must be administered by the lung to have their therapeutic effects. The preferred route for these compounds, by aerosol or instillation, has not been established. Antibiotics have also been given by this route, although documentation of their effectiveness and improved safety is minimal.

In nonintubated patients, it appears that only about 10 percent or less of the aerosolized drug actually reaches the airways or lungs. Alterations in breathing pattern (a slow inhalation and breath holding) may improve the delivery. Specific aerosol-generating devices have important effects, such as baffles and chamber shape, that have been shown to influence efficiency of drug delivery. Metered-dose inhalers and small-volume nebulizers have most frequently been used in intubated patients.

Larger particles tend to precipitate into the pharynx and upper airway of nonintubated patients. The drug they contain is rapidly absorbed and accounts for some of the therapeutic as well as most of the toxic effects seen. The appropriate balance between the amount of drug effects seen by the local and systemic routes of administration is not known and varies between patients, drugs, and devices. It is assumed that the systemic effects are undesirable; however, these may account for important, therapeutic effects.

The amount of drug delivered to the lung through an endotracheal tube appears even less than that seen with spontaneous breathing, although most reported studies suffer methodologic limitations. Caution should be applied when physiologic end points are used to compare intubated to nonintubated aerosol delivery. As mentioned above, systemic effects of drug delivered to the upper airway contribute to the measured effect. Drug impacting on the endotracheal tube wall may eventually reach the tracheal mucous (during saline solution instillation for suctioning, for example) and be absorbed. In short studies, this contribution to desired effect and toxicity will be unnoticed.

There are excellent methods to study drug delivery and deposition. Smaldone and colleagues have used radioactive-labeled serum albumin in combination with perfusion scanning to study the lung deposition of pentamidine in patients with HIV. This study demonstrated that nebulizer effects predominated over patient effects in drug delivery. Uniform lung distribution was also seen regardless of the degree of disease. The most important variable determining amount of drug was delivery fraction (amount of drug remaining in the lung); this was primarily influenced by the type of nebulizer and connecting tubing. This elegant method should be used in intubated patients to confirm these important observations.

The following questions were raised at a recent aerosol consensus development conference: What are the optimal ventilation parameters for inhalation treatment? Is spontaneous ventilation superior to