

Ethical Comparison of Living Donor Kidney Transplantation and Restored Kidney Transplantation

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1. Introduction

At the end of July 2012, 12,309 were registered with the Japan Organ Transplant Network as seeking renal transplantations. These patients are waiting for transplantations from donors who are brain-dead or cardiac arrested. There were only 211 such operations in this nation in 2011. It reportedly takes an average of about 14 years for patients to receive transplantation after registration, and surprisingly about 500 patients are waiting over 20 years. Some of the patients have removed their names from the waiting list, giving up due to their age and other reasons. As such, about 20,000 patients are believed to die every year while waiting for transplantation^[1]. Because of the diminutive availability of cadaveric donor organs, kidneys must be procured from living donors. The Japan Society for Transplantation stipulates in its ethics guidelines that transplants with living donors are limited to patients' relatives^[2]. In 2007, 1,037 renal transplantations from living donors were conducted which were about 85 % of all renal transplantation in Japan. Consequently the degree of dependence on transplantations from living donors is high compared with international norms. In our previous study^[3], some donors felt that they had no choice but to donate a kidney in order to save the recipients' lives, despite the risk to the donor. As the third choices, transplantation using a previously cancerous donor kidney which restored surgically may offer some relief of pressure on family members to donate.

2. Chronic Kidney Disease

The kidney's function is to filter the blood. All the blood in our bodies passes through the kidneys several times a day. The kidneys remove wastes, control the body's fluid balance, and regulate the balance of electrolytes. As the kidneys filter blood, they create urine, which collects in the kidneys' pelvis -- funnel-shaped structures that drain down tubes called ureters to the bladder. Each kidney contains around a million units called nephrons, each of which is a microscopic filter for blood^[4]. Chronic kidney disease (CKD)^[5] is a progressive loss in renal function over a period of months or years. The symptoms of worsening kidney function are unspecific, and might include feeling generally unwell and experiencing a reduced appetite. Often, chronic kidney disease is diagnosed as a result of screening of people known to be at risk of kidney problems, such as those with high blood pressure or diabetes and those with a blood relative with chronic kidney disease. There is no specific treatment unequivocally shown to slow the worsening of CKD. Severe CKD requires one of the forms of renal replacement therapy; this may be a form of dialysis, but ideally constitutes renal transplantation.

3. The Present Remedies for Chronic Kidney Disease

Dialysis is a process for removing waste and excess water from the blood, and is primarily used to provide an artificial replacement for lost kidney function in people with renal failure. In 4-5 hours, dialysis corrects the abnormality of the blood which accumulated during last 2 to 3 days. Many patients who receive dialysis in a centre are either unable to work or choose not to work due to the time required for travel and treatment. Even though, dialysis is an imperfect treatment to replace kidney function, as the kidneys are not

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only filtrating waste matters, but also reabsorbing, excreting, producing hormones, activating vitamin D, and metabolizing drugs, etc. It performs only about 10-15 % of the work a functioning kidney does.

Renal transplantation is an operation that places a healthy kidney in the body. The new kidney is placed inside patient's lower belly. The blood flows through the new kidney, which makes urine just like own kidneys did when they were healthy. Renal transplantation can replace complete kidney function.

Quality of life of patients with end kidney disease is influenced by the disease itself and by the type of replacement therapy. Dialysis must be repeated frequently and continued life-long until death or transplantation. Transplantation can alter quality of life positively. Most patients say the quality of their lives is better with renal transplantation than with dialysis. Patients who receive renal transplantation typically live longer than those who stay on dialysis. Patient survival rate after 15 years is 78% in living renal transplantation, and 71% in cadaveric renal transplantation. On the other hand, its rate in dialysis is only 29%. However, there is a shortage of organs available for donation. Many people who are candidates for renal transplantation are put on a transplant waiting list and require dialysis until an organ is available^[6].

Also in terms of cost-effectiveness, renal transplantation is better than dialysis. The study conducted by the University Maryland School of Medicine determined in 184 transplant patients that around 2 years and 8 months, a patient who opted for transplantation instead of continuous kidney dialysis saved \$27,000 per year in expenses^[7].

4. Results

4.1. Japanese special Circumstances in Transplantation

Thousands of patients in Japan are waiting for transplantations from donors who are brain dead or clinically dead, but whose organs are still usable. Only 182 such operations were performed in this nation in 2011^[6]. Patients wait an average of approximately 14 years to receive transplantation after registration on the waiting list. About 500 patients have waited over 20 years on this list^[6]. Some patients have chosen to remove their names from the list; these patients have given up because of advanced age or other reasons. Approximately 20,000 patients are believed to die every year in Japan while awaiting transplantation^[1]. The number of cadaveric renal transplantations is extremely low in Japan compared to that in the United States and some European nations. Compared to that in Japan, the waiting period for transplantation in the USA and Europe is much shorter (3–4 years and 3 years, respectively)^[8].

4.2. The Ethical Issue in Living Donor Transplantation

The ethics of living donor transplantation have been considered acceptable since the widespread use of live donor nephrectomy for renal transplantation. As surgical techniques and outcomes have improved, this practice has expanded. However organ donation by living donors presents an ethical dilemma, in that physicians must risk the life of a healthy person to save or improve the life of a patient. The core of the Hippocratic Oath of professional medical ethics is first Non-Maleficence. On this basis, living organ donation seems morally contestable. However, since this is done on the donor's request and for the physical benefit of the recipient, the principle of respect for the donor's autonomy and the principle of beneficence in the recipient generally outweighs than the infringement of the principle of Non-Maleficence. Most existing regulations provide that removal of organs from a living person may be carried out solely for the therapeutic benefit of a recipient and where there is no suitable organ or tissue available from a deceased person and no other alternative therapeutic method of comparable effectiveness, and that the removal of an organ may not be carried out if there is a serious risk to the life or health of the donor.

There are potential risks and benefits to the donor and recipient. With regard to benefits, there is a potential psychological benefit for the donor related to the altruistic act of giving. The recipient benefits from the superior quality of the organ. As a risk, the recipient's immune system would treat a transplanted kidney as a non-self and immediately or chronically reject it. Thus, having medications to suppress the immune system was essential. Suppressing individual's immune system places that individual at greater risk of infection and cancer, in addition to the side effects of the medications. In kidney donation, serious complications occur with major surgery such as nephrectomy, and perioperative mortality has been reported in about 1 out of 3000 living donor nephrectomies. The results have probably improved over time as for

surgery in general. As long-term morbidity, potential risks associated with kidney donation are hypertension and kidney impairment^[9].

The decision about whether or not to donate should be made by the potential donor. In addition, a potential donor has the moral right to take a reasonable risk in order to benefit recipient substantially. An organ may be removed from a living donor only after the person has given free, informed, specific consent. Almost all the donors went through a remarkably similar decision-making process when confronted with the idea of donating a kidney. They stated that the decision was made instantaneously when the possibility of kidney transplantation was first mentioned^[3,10]. It was not a cognitive decision; it came from the heart. It was an emotional and impulsive decision. The donors were not really interested in the instructions and explanations in the informed consent documentation. The donors did not want to hear about the risks to themselves and the recipients. They wanted to make the decision to save the recipients and convinced themselves that they were going to be fine. To some extent, informed consent is a myth. Donors hear very little of what medical personnel explain when they have already made up their minds to donate a kidney. Therefore, psychological support after donation is probably more important than pre-evaluation assessment.

It can be argued that when a patient is in dire need, there is always some form of coercion present. The donor should be given opportunity at any time during the evaluation and up to the point of donation to withdraw from the process without feeling guilty. Careful assessment of the psychosocial situation may help identify the reluctant donor and avoid this situation. In living organ donation every case is different. It must be handled with care. From an ethical point of view, the most important task today is to implement psychological counselling procedures to ensure that both donor and recipient are enabled to decide self-responsibly whether or not the transplantation should be performed. These procedures must also offer and protect the option to choose not to participate without being stigmatized by anyone. A recent study by University of Minnesota stated that 40% of their living donors felt at least some pressure to donate, and the amount of that pressure correlated with a donor's relation to their recipient^[11]. Also in our previous study^[3], some donors felt that they had no choice but to donate a kidney in order to save the recipients' lives, despite the risk to the donor.

4.3. Restored Kidney Transplantation

Patients have been known to resist the idea of receiving a previously cancerous kidney. However medical transplantation originally started and has been developed with an outlook that regards human bodies as medical resources. Utilizing kidneys discarded for cancer and other diseases is consistent with this outlook in terms of "recycling unwanted resources"^[12].

Because of the reduced quality of life experienced by dialysis patients, the high risk of mortality for patients on long-term dialysis, and the extremely long waiting list for transplantation, the option of restored kidney transplantation may be an attractive alternative for some patients. In many cases, total nephrectomy was performed even for small (≤ 4 cm) renal tumors. In a previous clinical study, ten of these nephrectomized kidneys were successfully transplanted to unrelated recipients after surgical restoration^[13]. Recipients in this clinical trial were selected on the basis of blood group match, high clinical evaluation scores, and negative results of cross-match testing. The term "match" refers to 6 possible HLAs. Before treatment with antirejection medications, 6 out of 6 antigens must match for successful transplantation^[14].

Some concern has been expressed regarding the possibility of transmitting disease after restored kidney transplantation. Many urologists are concerned about issues of immune suppression surrounding restored kidney transplantation. For example, melanoma and many other cancers are more likely to develop in immunosuppressed patients^[16]. However, others see the risk as minimal and recurrence of cancer as extremely unlikely in nonimmunocompromised patients. One study revealed the risk of tumor recurrence in the same site to be as low as 0.5% in patients who underwent partial nephrectomy^[15]. In addition, *de novo* tumor growth in the same kidney occurred in only 0%–6% of patients according to studies^[16]. Thus, kidneys restored after radical nephrectomy may be expected to have similarly low rates of tumor growth and recurrence in transplant recipients. The relation of newly developed cancers to previous renal cancers in either kidney is uncertain. On the other hand, in chronic dialysis patients, cancer risk is increased by 10%–80% than in the general population, according to several studies^[17].

We believe that the shortage of donors and the enormous negative impact on quality of life of patients with chronic kidney disease on dialysis outweighs the risk of possible cancer recurrence or disease development in the transplanted kidney. Ethical considerations necessitate informing the patient of the status of the kidney prior to obtaining consent for the procedure. Patients on the waiting list are emotionally very vulnerable. During counselling, data must be provided to demonstrate the statistical possibilities of cancer recurrence in restored kidneys. A maximum 6% chance of developing *de novo* cancer is a better statistic than a mortality rate of 40% during 5 years of dialysis^[18]. In the event that cancer does recur in the donated organ, partial nephrectomy can again be performed. This is still advantageous from the point of view of long-term survival compared to dialysis.

In countries like Japan, where the demand for donated kidneys far exceeds the supply, transplantation using a previously cancerous donor kidney may offer some relief of pressure on family members to donate. Recipients may also feel better about not having to ask family members to be donors. Using restored kidneys resulting from nephrectomy because of cancer alleviates this problem to some extent. Other problems in Japan include kidneys donated through an illegal trade, faked adoption, or illegal transplant surgery using kidneys donated by foreigners in developing countries. These problems could also be avoided by restored kidney transplantation. Transplantation of kidneys that have been restored after resection of cancerous lesions may also aid in solving the ethical dilemma that many doctors face when potential donors want to back out at the last minute. As advocates for both patients and donors, they may find themselves having to inform families that donors have changed their minds about donating. Rather than putting donors in such a difficult position, the temptation may arise to take the blame for a nonexistent error in order to protect family relationships and the present and future health (both mental and physical) of the potential donor. Previously-cancerous donor kidneys that have been restored after nephrectomy may be added to the donor pool to relieve the pressure on families, doctors, and transplant recipients.

5. Conclusion

Organ donation is a stressful experience. Donors' psychological states must be assessed in terms of their ability to handle stress and depression. Psychiatric support is more crucial after donation. In hospitals with programs on living donors, a social worker or psychologist must be available to address post-transplantation issues and concerns. Many people still rely on emotion and not intellect to guide them in decision making about donation. Thus, Japanese public policy and transplant centres should take a more proactive role in screening and evaluation of prospective donors.

Over the past decade, stem cell research has advanced progressively and significantly. The kidney has the potential to regenerate itself provided that the damage is not too severe and the kidneys structure remains intact^[19]. However, clinical application isn't the near future. In order to eliminate the organ shortage at present, we think the concept of using restored kidneys for transplantations, including those affected by cancer, may be one option. Based on the standpoint of donors, it is more rational to use diseased kidneys than it is to take important kidneys out of healthy people by invasive surgery because removed kidneys are of no use to the previous owner. If this is the time when the effective and recycled use of human bodies is inevitable, we need to have serious discussion with an eye to the effective utilization of medical resources.

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