Iranian Model of Paid and Regulated Living-Unrelated Kidney Donation

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Since the 1980s, many countries have passed legislation prohibiting monetary compensation for organ donation. Organ donation for transplantation has become altruistic worldwide. During the past two decades, advances in immunosuppressive therapy has led to greater success in transplantation and to increased numbers of patients on transplant waiting lists. Unfortunately, the altruistic supply of organs has been less than adequate, and severe organ shortage has resulted in many patient deaths. A number of transplant experts have been convinced that providing financial incentives to organ sources as an alternative to altruistic organ donation needs careful reconsideration. In 1988, a compensated and regulated living-unrelated donor renal transplant program was adopted in Iran. As a result, the number of renal transplants performed substantially increased such that in 1999, the renal transplant waiting list was completely eliminated. By the end of 2005, a total of 19,609 renal transplants were performed (3421 from living related, 15,356 from living-unrelated and 823 from deceased donors). In this program, many ethical problems that are associated with paid kidney donation also were prevented. Currently, Iran has no renal transplant waiting lists, and >50% of patients with ESRD in the country are living with a functioning graft. In developed countries, the severe shortage of transplantable kidneys has forced the transplant community to adopt new strategies to expand the kidney donor pool. However, compared with the Iranian model, none of these approaches has the potential to eliminate or even alleviate steadily worsening renal transplant waiting lists.

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In the past three decades, advances in immunosuppressive therapy and organ transplant technology have improved patient and graft survival rates in renal transplant recipients. Available data show that renal transplantation, not dialysis, has become the treatment of choice for ESRD (1). Because transplantation significantly prolongs patient survival and improves the quality of life compared with dialysis therapy, the number of patients who ask for a renal transplant rather than dialysis has steadily increased. Unfortunately, the supply of transplantable kidneys has been much less than the demand. As a consequence, the number of patients who are on renal transplant waiting list for deceased-donor transplantation has increased continuously, and each year, thousands of patients die while waiting for renal transplantation.

The main reason for this increasing number of patients who are on the renal transplant waiting list is the steady growth of a patient population that needs renal replacement therapy worldwide. At the end of 2001, approximately 1,479,000 people were alive in the world just because they had access to dialysis and renal transplant facilities. This number increased to 1,783,000 by the end of 2004. The major factors that contribute to this continuous growth in the number of patients with ESRD has been explained by universal aging of populations, higher life expectancy of treated patients with ESRD and increasing access to dialysis and renal transplantation facilities of a generally younger patient population from developing countries. The effective strategies to prevent increasing numbers of patients with ESRD or new treatment modalities to be either superior or alternative to dialysis and renal transplantation are not expected to be available at least in the upcoming decade (2,3).

Since the 1980s, many countries have passed legislation prohibiting monetary compensation for organ donation for transplantation. All organ donations have become altruistic, meaning that there are no financial incentives to people who are willing to have their organs or organs of their deceased family members used for transplants. An ethical consensus has developed around the world that there should be no payment for transplantable organs from either living or deceased individuals. Unfortunately, the altruistic supply of organs has been less than adequate, and the results of this altruistic system have met with limited success. During the past two decades, several approaches have been adopted to increase altruistic organ donations, but the gap between supply and demand has worsened over time. Some experts believe that the use of self-interest (*i.e.*, financial incentives) to shape human behavior is much better understood than the use of altruism. Only under certain and limited circumstances does the human being show willingness for uncompensated transfers and generosity toward others, whereas the forces of self-interest are basic for almost all of our daily activities. This is the main reason that efforts to use altruism for organ donation have met limited

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success and why by providing financial incentives to organ sources, it is expected that the number of available organs for transplantation will increase (4,5).

Because the organ shortage has become more severe worldwide, some from the transplant community believe that altruism alone is not enough to satisfy the needs of the thousands of patients who are on renal transplant waiting lists and that providing some financial incentives or social benefits is necessary to increase the number of deceased or living organ donations. Some transplant clinicians also believe that prohibition of all forms of financial incentives to organ sources should not be considered an ethical attitude (6).

In 1988, a compensated and regulated living-unrelated donor renal transplant program was adopted in Iran. As a result, the number of renal transplant centers and renal transplantations that were performed rapidly increased such that by 1999, the renal transplant waiting lists in the country was eliminated successfully (7,8). By the end of 2005, a total of 19,609 renal transplants were performed. This approach eventually was named the Iranian model renal transplant program. Currently, Iran has no renal transplant waiting lists, and >50% of patients with ESRD in Iran are living with a functioning graft.

In this article, first we review the backgrounds, characteristics, results, and ethical issues surrounding the Iranian model paid kidney donation program showing how the renal transplant waiting list in Iran has been eliminated successfully. Finally, we briefly discuss other strategies that have been adopted around the world to increase organ donation, including transplantable kidneys.

Background and Development of the Iranian Model

Iran, in ancient Greek sources called "Persia" or "The Land of Aryans," had a higher degree of civilization during the entire period of the first millennium B.C. and now is a developing country located in the Middle East between the Caspian Sea and the Persian Gulf. It covers 1,648,000 km^2 and has 68 million inhabitants. Iran's gross domestic product per capita is $7219 USD with a total health expenditure of 6% of its gross domestic product. The prevalence of patients with ESRD in Iran is approximately 25,000, or 370 patients per million.

The first renal transplantation was performed in Iran in 1967. From 1967 to 1988, the number of patients who were undergoing dialysis steadily increased, but the renal transplantation program severely lagged in growth in comparison with dialysis. Between 1967 and 1985, only approximately 100 renal transplants were performed. Since 1980, because of very limited renal transplant activity in the country, the Ministry of Health started allowing dialysis patients to receive transplants abroad with governmental funds. Any dialysis patient who had a letter of acceptance from a transplantation unit abroad was accepted as a transplant candidate and all travel and transplant expenses were paid. As a result, a large number of patients who were undergoing dialysis and wishing to receive a transplant created a long renal transplant waiting list at the Ministry of Health. Between 1980 and 1985, more than 400 of these patients traveled to European countries and some to the United States using governmental funds and received a renal transplant. The majority of these transplants were performed in the United Kingdom from living-related donors. In 1985, the high expense of renal transplantation abroad and the increasing number of patients who were on the renal transplant waiting list prompted health authorities to establish renal transplant facilities inside the country. Two renal transplant teams were organized, and between 1985 and 1987, a total of 274 renal transplants from living-related donors were performed (7,8).

In 1988, a large number of patients with ESRD needed renal transplant but had no living-related donor. The deceased-donor organ transplantation program had not been established, and it did not seem as though it would be started effectively any time in the near future. The patients had created a long renal transplant waiting list at the Ministry of Health to travel abroad with governmental funds for transplantation. Transplantation of so many patients abroad was very expensive and understandably unaffordable. Therefore, a government-funded, -regulated, and -compensated living-unrelated donor renal transplantation program was adopted in 1988. As a result, the number of transplant teams increased from two to 25. The number of renal transplantations that were performed increased rapidly such that by 1999, the renal transplant waiting list was eliminated (7,8). By the end of 2005, a total of 19,609 renal transplantations were carried out (3421 from living-related donors, 15,365 from living-unrelated donors, and 823 from deceased donors). Figure 1 shows the annual number of renal transplants that were performed in Iran from 1984 to 2005. Renal transplant activity in Iran has reached 28 renal transplants per million per year. More than 78% of all renal transplants have been from living-unrelated donors.

Characteristics of the Iranian Model

In the Iranian model renal transplant program, during evaluation of all renal transplant candidates, the transplant physician emphasizes the advantages of living-related donor compared with living-unrelated donor renal transplant and recommends renal transplantation from a living-related donor. He also discusses the scarcity of deceased-donor kidneys in the country. If the patient has no living-related donor or the potential donor would not be willing to donate a kidney, then the patient is referred to Dialysis and Transplant Patients Association (DATPA) to locate a suitable living-unrelated donor. (Only a transplant center at Shiraz University with active deceased-donor liver and kidney transplantation program asks all renal transplant candidates to wait up to 6 mo for possible deceased-donor renal transplantation.) Those who volunteer as living-unrelated donors also contact DATPA. All members of DATPA are patients who have ESRD and receive no incentives for finding a living-unrelated donor or for referring the patient and donor to a renal transplant team (Figure 2). Currently, there are 302 dialysis units, 25 transplant centers, and 79 DATPA offices all over the country. There is no role for a broker or an agency in this program. All renal transplant teams belong to university hospitals, and the government pays all of the hospital expenses of renal transplantation. After renal transplantation, the living-unrelated donor receives an award and health insurance from

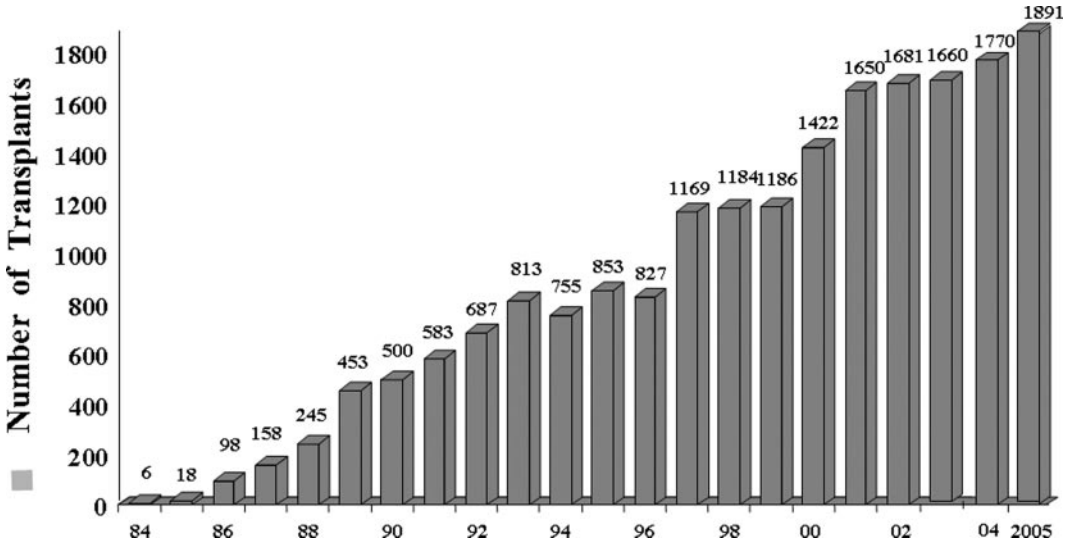

Figure 1. Annual number of renal transplants performed in Iran from 1984 to 2005.

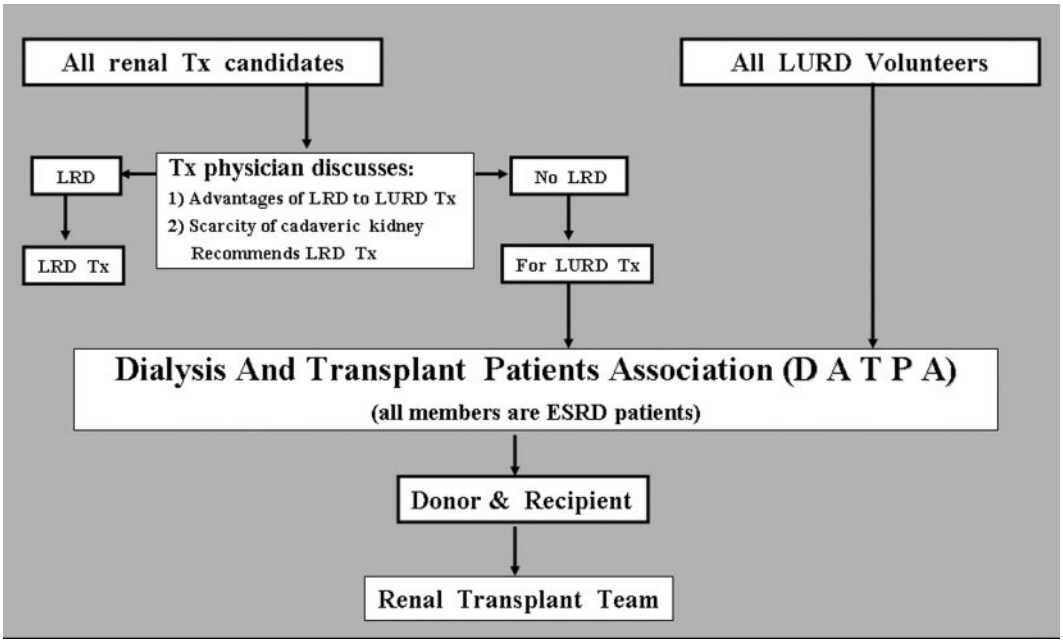

Figure 2. Role of Dialysis and Transplant Patients Association (DATPA) on paid kidney donation program. LURD, living-unrelated donor; LRD, living-related donor; Tx, transplantation.

the government. A majority of living-unrelated donors also receive a rewarding gift (arranged and defined by DATPA before transplantation) from the recipient or, if the recipient is poor, from one of the charitable organizations. The government also provides essential immunosuppressive drugs such as cyclosporine Neoral and mycophenolate mofetil to all transplant recipients at a greatly subsidized and reduced price. Charitable organizations also are very active in providing these drugs or in paying any expenses of renal transplantation to poor patients. Renal transplant teams receive no incentives from the recipient or from the government's award. The program is under the close scrutiny of the transplant teams and the Iranian Society for Organ Transplantation regarding all ethical issues. To prevent transplant tourism, foreigners are not allowed to undergo renal transplantation from Iranian living-unrelated donors. Also, they are not permitted to volunteer as kidney donors to Iranian patients. Foreigners can receive a transplant in Iran, but the donor and the recipient should be from the same nationality, and authorization for such transplantation should be obtained from the ESRD Office of the Ministry of Health (7,8).

Donor and Recipient Evaluation

The donor and the recipient evaluations in all transplant centers are very similar. In our transplantation unit at the

Hashemi Nejad Kidney Hospital in Tehran, the selection and the preparation of all potential renal transplant recipients and living kidney donors are carried out by complete clinical and psychological evaluation as well as by performing appropriate laboratory tests and imaging. Recently, the European Best Practice Guidelines for Renal Transplantation and the Amsterdam Forum on the Care of the Live Kidney Donor Medical Guidelines are being used for this purpose (9,10). From 1986 through 2000, for all living kidney donors, a voluntary consent was assessed by the "Donor Selection Panel," which consists of nephrologists, transplant surgeons, and members of nursing staff to exclude the possibility of pressure being exerted for kidney donation. Since 2000, the evaluation and the selection of potential donors and recipients has been carried out independently, first by transplant nephrologists, then by members of the surgical team. In selecting living-related donors, priority is given to the donor who has a better HLA match with the recipient. For living-unrelated donor transplants, HLA matching is not practical because the Iranian model is a directed kidney donation program, so any donor who is ABO compatible with the patient is accepted for evaluation.

Immunosuppressive Drugs

Before 1996, the available immunosuppressive drugs consisted of cyclosporine Neoral, generic azathioprine, and prednisone. Since 1996, mycophenolate mofetil has been used increasingly instead of azathioprine and by 2004 has almost replaced it. The government imports and greatly subsidizes these essential immunosuppressive drugs (Neoral, CellCept, azathioprine, and prednisone) and makes those available to all transplant recipients in a very reduced price. All patients with ESRD including renal transplant recipients belong to a group of patients called "Patients with Special Diseases" and are eligible for a government-provided medical insurance. As a result, the majority of transplant recipients receive these immunosuppressive drugs free. The remaining patients pay for these drugs a little money per month. If a transplant recipient is poor and could not afford the drugs, then the charitable organizations will pay for it. This is one of the reasons that all patients, either poor or rich, have equal access to renal transplantation in Iran. For high-risk cases (*e.g.*, those undergoing a second transplant, those with previous high panel reactivities), induction therapy with anti-thymocyte globulin and rarely with IL_2 receptor antibodies is carried out. Antirejection therapy consists of methylprednisolone (1 g/d) for 3 to 5 d and anti-thymocyte globulin in patients with steroid-resistant rejection. IL_2 receptor antibodies, tacrolimus, sirolimus, and OKT_3 are neither subsidized by the government nor covered by insurance and so are very expensive and are used very rarely. As a result, individualization and tailoring of immunosuppressive therapy remains very limited.

Demographics and Outcome Data of Renal Transplantations

Unfortunately, there is no national transplant registry in Iran to report the short- and long-term results of transplantation in all transplant recipients and kidney donors. Most renal transplant teams report their own results as single-center experiences (11–13). The ESRD Office of Iran has only demographic data but lacks the short- and long-term results of transplantation, so the results from the Hashemi Nejad Kidney Hospital (a pioneering transplant center and one of the largest in Iran) are given next as an example for the whole country.

Between April 1986 and January 2006, a total of 1995 renal transplants were performed in this hospital. A total of 496 (25%) were from living-related donors, and the remaining 1499 (75%) were from living-unrelated donors. A total of 743 (37%) recipients were female, and 1252 (63%) were male. Their ages ranged from 8 to 68 yr. In one of our studies we reported a significant gender disparity in living-unrelated (paid) kidney donors (91% male, 9% female; age range 21 to 37 yr) (14).

In a recent data analysis, the overall patient survival rates were 93.8, 87.8, and 76% and the overall graft survival rates were 90.4, 75.4, and 52.8% at 1, 5, and 10 yr, respectively. There were no significant differences in graft survival rates between recipients of one HLA haplotype–matched living-related donor and living-unrelated donor recipients ($P = 0.35$). In living-unrelated donor renal transplant recipients, the patient survival rates were 93.9, 87.1, and 72.2% and the graft survival rates were 90.5, 74.4, and 48.8% at 1, 5, and 10 yr, respectively (Figure 3).

Elimination of the Renal Transplant Waiting List

The Iranian model of regulated paid kidney donation has eliminated the renal transplant waiting list in the country. In Iran, as in other developing countries, the prevalence of patients with ESRD is markedly lower compared with the prevalence of patients who are on renal replacement therapy in developed countries. A major cause of this is the many patients who are from villages and small towns and do not receive a diagnosis and are not referred for dialysis therapy. There also is no adopted restricting policy for accepting patients with ESRD for renal transplantation; however, the low prevalence of patients with ESRD results in fewer numbers of transplant candidates. This is the main reason that the renal transplant waiting list was eliminated quickly and successfully in Iran.

At the end of 2004, the prevalence of patients with ESRD was

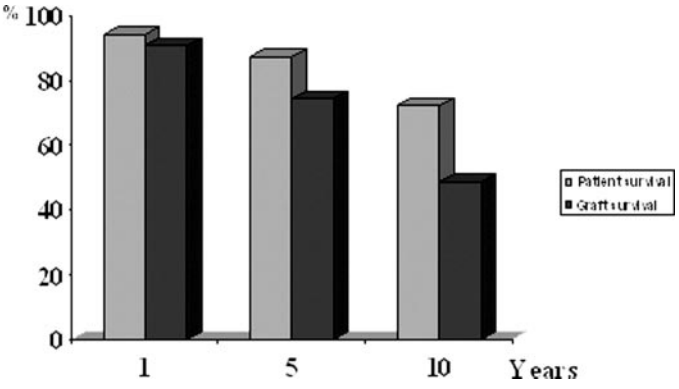

Figure 3. Results of 1499 living-unrelated donor renal transplants in Hashemi Nejad Hospital–Tehran. ▨, patient survival; ■, graft survival.

2045 per million people (pmp) in Japan, 1505 pmp in North America, 585 pmp in Europe, 380 pmp in Latin America, 370 pmp in Iran, and 190 pmp in the Middle East (3). As expected, in countries with higher ESRD prevalence values, more patients are on renal transplant waiting lists, and this is why a renal transplant activity of 25 to 28 pmp has eliminated the renal transplant waiting list in Iran, whereas much higher renal transplant activities have not done so in North America and European countries.

Ethical Issues Surrounding the Iranian Model

The ethical issues that are related to the Iranian model of paid kidney donation are presented in two parts. In the first part, the ethical issues that support the Iranian model are discussed, showing that the many ethical problems that arise from paid kidney donation have been prevented in this transplantation model. In the second part, several ethical problems that still remain in Iranian model are mentioned, emphasizing that public education and further governmental funding for living paid kidney donors and providing some social benefits to them will make the Iranian model ethically more acceptable. At that time, the revised form of this kidney donation model can be implemented at least in some developing countries to prevent many patient deaths and suffering (15).

Ethical Issues Supporting the Iranian Model

As mentioned, there is no role for a broker or an agency in this transplantation program. The association for patients with ESRD is a charitable organization and receives no incentives from donors or recipients. The government pays for all hospital expenses of renal transplantation. The medical and surgical fees for transplantation are greatly lower compared with the fees for similar services.

All transplant candidates who are poor receive renal transplantation. The elimination of renal transplant waiting lists means that all patients with ESRD, either rich or poor, have equal access to renal transplant facilities; otherwise, many poor patients would remain on the renal transplant waiting list. The main reason for this equal access is the active role of charitable organizations that pay for many expenses of renal transplantation that the poor patients cannot afford. One of the arguments against paid kidney donation is that the kidney donors are almost poor and illiterate, whereas the majority of recipients are educated and wealthy. We previously conducted a study on 500 renal transplant recipients and their living-unrelated donors to determine which socioeconomic classes are receiving transplants more from paid kidney donors (16). All of these donors and recipients were grouped according to their level of education, which showed no significant differences. In this study, 6.0% of living-unrelated donors were illiterate, 24.4% had elementary school education, 63.3% had a high school education, and 6.3% had university training. Corresponding levels in their 500 recipients were 18.0, 20.0, 50.8, and 11.2%, respectively. Then they were grouped according to whether they were poor, rich, or middle class. The results showed that 84% of paid kidney donors were poor and 16% were middle class, and of their recipients, 50.4% were poor, 36.2% were middle class, and 13.4% were rich. So >50% of kidneys from paid donors were transplanted into patients from poor socioeconomic class. This finding is a clue against commercialism in the Iranian model renal transplant program.

The paid kidney donation model did not inhibit the establishment of a deceased-donor organ transplantation program. Since April 2000, when legislation that was passed by parliament accepting brain death and deceased-donor organ transplantation, the annual number of cadaveric kidney, liver, and heart transplants has increased steadily in the country. In 2000, only 1.8% of all renal transplants were from deceased donors. This increased to 12% in 2004 and 2005 (Figure 4). This slow increase in deceased organ donation is due to infrastructural deficiencies and cultural barriers in the country as well as to administrative incapabilities of health authorities rather than being all because of availability of the paid kidney donation program.

This program probably has eliminated the many coercive living-related donor renal transplants. Before 1988, almost all renal transplants in Iran were from living-related donors. Since adoption of this transplantation model, the number of living-related donor transplants has decreased (in 2005, only 12% of all renal transplants were from related donors). We believe that this decreasing number has been due partly to elimination of coercive living-related donor transplants and partly to availability of the paid kidney donation program. Because of cultural reasons, coercive living-related donor renal transplants are common in most developing countries, including Iran; we believe that with a compensated and regulated living-unrelated donor renal transplantation program in place, it may be more ethical to perform a paid renal transplantation from a volunteer living-unrelated donor than from a living-related donor or spouse who is under some degree of family pressure or with emotional coercion.

The Iranian model of paid kidney donation also has eliminated the many illegal and commercial renal transplants. Before 1988, a number of patients who had no living-related donors traveled India, where they received paid renal transplants. The majority of these bought transplants were associated with transmission of hepatitis and surgical complications. Several other patients traveled together with their unrelated donors to European countries and received a transplant. In a few of these

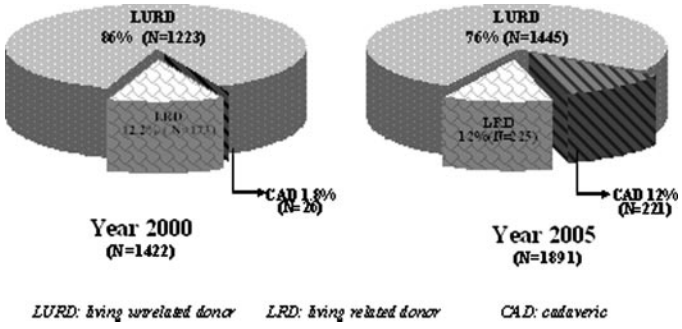

Figure 4. Sources of kidney donations in Iran in 2000 and 2005.

cases, the transplant documents were prepared carefully as though the kidneys were being given altruistically by living-related donors. The adoption of the legalized and compensated living-unrelated donor renal transplant program in 1988 eliminated the need for Iranian patients for commercial or illegal paid transplants abroad. Shortly after adoption of the Iranian model of kidney donation, several wealthy patients from Arabic countries came to Iran and received transplants from Iranian paid donors. Transplantations were performed by surgeons who, unfortunately, had no accurate understanding of ethical issues regarding organ transplantation. A kidney market for transplant tourism was nearly to flourish in the country. As a result, the Iranian Society for Organ Transplantation made a regulation and sent it to the Ministry of Health and transplant centers that no foreigners are allowed to undergo renal transplantation from Iranian kidney donors. This amendment prevented the development of transplant tourism in Iran.

We previously conducted a study on nationality of transplant recipients and kidney donors in 1881 consecutive renal transplants in our center. Nineteen (1%) recipients were refugees, and 11 (0.6%) were other foreign nationals who received kidneys from living-related donors or from living-unrelated donors of the same nationality. Of 1881 renal transplant recipients, 18 (0.9%) also were Iranian immigrants (residing abroad for years) who came and received kidneys from Iranian paid donors. Transplantation of these 18 patients was true transplant tourism. The scale of this form of transplant tourism is very small (<1%) in the Iranian model; however, it is under ethical evaluation (17).

During the past two decades, because of 23 yr of civil war in Afghanistan (1978 to 2001) and 8 yr of the Iran-Iraq war (1980 to 1988), Iran has hosted approximately 0.5 million Iraqi refugees in its western provinces and approximately 2.5 million Afghan refugees in its eastern provinces and major urban centers. The majority of these refugees have lived outside camps, having access to the Iranian labor market and a number of government services such as dialysis and renal transplant facilities. In June 2004, we conducted a study to investigate the access of Afghan refugees to Iranian transplant centers as kidney donors and recipients (18). At that time, 1.6 million refugees still remained in Iran. This study showed that 241 refugees had ESRD (179 were undergoing dialysis, and 62 had renal transplantation in Iran). Kidney donors for these 62 transplant recipients were living-related donors in nine, spouses in two, Afghani living-unrelated donors in 50, and deceased-donor kidney in one. Afghan refugees are among the poorest people in the world. In >15,000 living-unrelated donor renal transplantations performed in Iran, no refugee had donated a kidney to an Iranian patient. This study concluded that transplantation of all refugees in need and the absence of their use as kidney donors to Iranian patients proffer strong evidence against commercialism and a reason to believe that the Iranian model renal transplantation is practiced with ethical standards. There also is no doubt that by adoption of the Iranian model of regulated paid kidney donation, we have prevented many patient deaths and suffering in the country.

Ethical Problems Still Remaining in the Iranian Model

Because the amount of governmental donor award (approximately $1200 USD) is not enough to satisfy the majority of kidney donors, recipients provide rewarding gifts to donors. If the recipient is poor, then the rewarding gift is provided by charitable organizations. This also results in directed paid kidney donation, meaning that the transplant candidate and the volunteering kidney donor meet each other in a DATPA meeting for arrangement of rewarded gifting to be paid to the donor after transplantation. Providing sufficient financial incentives and some social benefits to each living-unrelated donor by the government will eliminate rewarding gifts and will make the Iranian model a nondirected paid kidney donation program whereby the donors and the recipients will not see and know each other at least before transplantation. All transactions for financial incentives will be carried out by organ procurement organizations (OPO). The OPO will receive all governmental donor award budgets as well as all charitable donations. The donor will donate a kidney to the OPO and will receive all defined financial incentives from the OPO. Because of lack of administrative expertise in health authorities, this approach has not yet been tested in the Iranian kidney donation model.

Unfortunately, the financial incentives to kidney donors in the Iranian model neither has enough life-changing potential nor has enough long-term compensatory effect, resulting in long-term dissatisfaction of some donors. However, providing adequate financial incentives to kidney donors and awarding some social benefits to them will eliminate almost all long-term dissatisfaction. Some opponents have sensationalized that the majority of Iranian paid kidney donors have been poor and have remained poor after kidney donation. As mentioned, in the Iranian model of paid kidney donation, not only the majority of donors (84%) but also the majority of transplant recipients (50.4%) also are from poor socioeconomic class. This national program is not adopted to upgrade the socioeconomic class of kidney donors and is very different from commercial transplants that are carried out in other countries.

The only social benefit that is awarded to Iranian kidney donors is health insurance. Providing more legal and social benefits to paid kidney donors, in addition to financial incentives, will satisfy them better in the long term. When an unrelated donor donates a kidney to a patient with ESRD, the intent also is to save or improve the life of another member of society. Therefore, the society should feel an obligation to provide compensation for this service. There are some legal and social items of benefits for war-injured veterans in each society. Several of these items can be legalized and offered to each kidney donor in addition to financial incentives as a token of appreciation and compensation by society (19).

Public education also is necessary to show the minimal risk of kidney donation and better outcome of living-related donor renal transplantation to increase the number of transplants from living-related donors. In one of the pioneering renal transplant centers in Tehran, laparoscopic live-donor nephrectomy is being taught and performed with encouraging results to increase the number of live kidney donations especially from related donors (20).

The cadaveric renal transplant activity can be increased substantially in the country if the health authorities give higher priority to the deceased-donor organ donation program. In the Shiraz University transplant center, where deceased-donor organ procurement is in higher priority as a result of an active liver transplant program, the number of cadaveric renal transplantations is the highest in the country (21). Finally, there is a need for establishment of a donor registry to study the long-term medical and socioeconomic consequences on all living kidney donors.

Other Reasons for Adopting and Continuing Regulated Paid Kidney Transplantation in Iran

Use of Altruism Has Failed to Alleviate Organ Shortage

In the 1980s, the shortage of transplantable organs was less severe than it is today, and the majority of transplant experts were optimistic that altruistic organ donation would be an effective strategy for alleviating or even eliminating organ shortage. This was the main reason that legislation prohibiting monetary compensation passed and organ donation became altruistic (4,5). Now, after two decades, it has become evident that considerable efforts to provide a sufficient supply of organs through altruism have met with limited success. Because the severe organ shortage has resulted in many patient deaths, a number of transplant experts have been convinced that providing financial incentives to organ sources as an alternative to altruistic organ donation needs careful reconsideration (22,23). For example, in 2001, several legislative proposals were submitted to the US Congress to promote organ donation. These proposals called for a donor medal of honor and a tax credit or tax refund upon donation of an organ from a living or deceased person. However, several influential senior experts in transplantation have urged the US Congress to retain the prohibition of monetary compensation for organ donation (24). Nevertheless, the previous severe condemnations by some ethicists against paid kidney donation is softening gradually; it is possible that some type of compensated living-unrelated donor renal transplantation also may be legalized in the United States or other developed countries in the future.

Renal Transplantation from Living-Unrelated Donors Is Steadily Increasing Worldwide

Because it has been shown that the outcome after living-unrelated donor renal transplants is the same as after one haplotype–matched living-related kidney transplants and superior to the outcome after deceased-donor renal transplants (25), in the United States, the number of renal transplants from living donors increased by 257%, from 1812 in 1988 to 6473 in 2003. Kidney donation increased substantially in all living donor groups, but the greatest increase was in altruistic, nonspousal living-unrelated donors. It is interesting that the percentage of living donors who were either spouse or unrelated to the recipient increased from 5% in 1988 to 33% in 2003 (26). In other countries, such as Canada, the number of living-unrelated kidney donors also has increased (27). Because the number of uncompensated living-unrelated donors has been very limited in Iran, the paid kidney donation program has been adopted to use this viable source of transplantable kidneys.

Proposals of Some Ethicists Regarding Shortage of Transplantable Kidneys Are Disappointing and Unacceptable

Even though so many patients worldwide die or suffer on dialysis needing renal transplantation, there still are many ethicists from developed and developing countries who are against compensated renal transplantation. These ethicists who support only altruistic organ donations have proposed that in developed countries, the solution is to increase renal transplant activity by accepting marginal donors or by passing presumed consent law, but the renal transplant waiting list is increasing steadily in developed countries, and many patients continue to die while waiting for a renal transplant. In the United States, the number of patients who are on the renal transplant waiting list increased from 23,604 in 1988 to 80,492 in 2003. The number of patients who died while waiting for a renal transplant also increased from 1133 (4.8%) in 1988 to 3944 (4.9%) in 2003 (28). In developing countries, the proposals of most transplant ethicists have been mainly to establish a Western model for deceased-donor organ transplantation with high renal transplant activity, but many infrastructural deficiencies (along with cultural barriers) in these countries prevent such a large-scale cadaveric renal transplantation program. Second, they propose to increase further living-related donor renal transplants, which surely will result in transplantation with coercion, particularly in female donors, a situation that is more unethical than the use of paid living kidneys. In a study by Muthusethupathi *et al.* (29) from India, in 125 first-degree related donor renal transplantations, 66% of kidney donors but only 17% of recipients were female.

Results of the Iranian Model of Paid Kidney Transplantation Are Encouraging

As mentioned, the patient and graft survival rates are the same as the results from conventional transplant centers. The donor morbidity and mortality also are comparable to international data. In more than 18,000 live-donor nephrectomies that were performed in Iran, there have been four (0.02%) perioperative donor mortalities in the whole country. This mortality rate is similar to what has been reported from the world's large series (30–32). The major and minor perioperative complications reported from our center were 1.5 and 8.5%, respectively (33). The long-term risks of kidney donation have not been studied in our center. There is a need for donor registry and funding. Only a few European transplant centers have living kidney donor registries. In the United States, even though more than four times the number of Iran live kidney donations are performed each year, the live kidney donor registry and the long-term outcome data in all living kidney donors are lacking.

Some studies have shown the lower risk for long-term mortality compared with an age- and gender-matched background population. This increased survival is not surprising because kidney donors are positively selected and screened for diseases (34). However, the effect of kidney donation on the long-term outcome of living donors has always been studied in terms of

increased renal death or renal morbidities. A long-term follow-up on a large number of living donors is necessary to ensure, for example, that kidney donation and drop of GFR has not predisposed living donors to increased cardiovascular events.

Regulated Paid Kidney Transplantation Has Prevented Illegal and Commercial Transplantations in Iran

Currently, all transplant candidates and their families are well informed that one's quality of life with a renal allograft is greatly improved over living with chronic dialysis (1) and that renal transplantation from living-unrelated donors is superior to that of deceased-donor transplants (25). It also has been shown that the shorter the period on dialysis, the better the patient and graft survival rates (35). For these reasons, many patients with ESRD want to receive a transplant quickly from living donors, rather than wait for years to receive a deceased-donor kidney. Some patients from developed countries are traveling abroad to buy kidneys from strangers in developing countries. Because of the shortage of transplantable kidneys and facing long waiting lists, some patients also have turned to Internet sites that offer the matching with living-unrelated kidney donors. Several patients have received transplants from donors that they found through www.MatchingDonor.com (36).

Iranian Model Is Very Different from Commercial Transplantations Carried out Elsewhere

Unfortunately, much of the transplant community's experience with paid kidney transplantation is from centers that have approached it with little regard to ethical standards. Before 1995, several thousand unregulated paid renal transplants were performed in India each year. The kidneys were sold by middlemen to wealthy patients who came not only from India but also from overseas. Poor donors were exploited by brokers and transplant teams, who received a major part of the money that came from the kidney sale. Almost all of these transplants were performed in private back-street clinics with incomplete donor and recipient evaluation and resulted in high incidence of surgical complications and transmission of infections (37,38). The Iran model of a regulated transplant program involves paid kidney donation, but the ethical aspects are strictly enforced by the transplant teams and the Iranian Society of Organ Transplantation.

Other Successful Strategies for Expanding the Kidney Donor Pool

The rapidly increasing number of patients who are on renal transplant waiting lists has forced the transplant community to look at new strategies to increase the number of transplantable kidneys. These strategies are as follows: Encouraging live-donor renal transplantation (from genetically related and emotionally motivated donors); passing presumed consent law; use of extended criteria (marginal) and non–heart-beating deceased donors (NHBDD); performing ABO-incompatible, paired-exchange renal transplantations; and accepting nondirected kidney donations. All of these strategies have been effective in expanding the kidney donor pool on a limited scale, but compared with Iranian model, none of these approaches has the potential to eliminate or even alleviate renal transplant waiting lists.

By using several strategies, the number of kidney transplants from living and deceased donors markedly increased during the past two decades. In the United States, the significant increase in renal transplant activity was due to the use of kidneys from living-related and living-unrelated donors. Renal transplants from living donors increased by 257%, from 1812 in 1988 to 6473 in 2003 (26). The largest increase was in kidney transplants from spouses and living-unrelated donors. The spousal transplants that led to the increase in unrelated donor renal transplants grew from 1995 to 2000. Since 2000, this has stabilized at approximately 700 transplants per year. The substantial increase was in the number of nonspousal, unrelated donor transplants, which grew by 1600%, from 73 in 1994 to 1250 in 2003 (39). The deceased-donor renal transplants increased only by 34%, from 7284 in 1988 to 9765 in 2003 (26). Nearly all of this modest increase came from acceptance of marginal or extended-criteria donors (ECD). However, the ECD renal transplants are associated with poorer outcomes. Even the ECD renal transplantation is no longer a rapidly growing source; it increased in the United States from fewer than 200 in 1988 to only 1200 in 2002 (40).

The use of NHBDD has grown since the report of their effectiveness was published (41). The rate of NHBDD kidney transplants varies from one country to another. This number increased in the United States from 106 in 1995 to 414 in 2003 (26). In Japan, the number of renal transplants from deceased donors is small, and most of these are from NHBDD (of 1324 deceased-donor kidney transplants, 45 were from heart-beating deceased donors and 1274 were from NHBDD) (42). In The Netherlands, during the past decade, the number of NHBDD kidney transplants has increased remarkably. Surprising, the number of heart-beating kidney transplants has diminished at the same rate, so the total number of annual renal transplants from deceased donors has remained the same. In Germany, transplantation from NHBDD is prohibited (43).

In countries such as Spain, Austria, Belgium, and Singapore, with "presumed consent" legislation, the rate of organ donation and kidney transplantation has increased substantially. This law mandates that every adult individual who dies is a potential donor unless during his life he specifically declines to participate (44). The proposal of presumed consent was not tested for its effectiveness in the United States and many other countries because it is considered against the autonomy of families of deceased donors.

Currently, the Spanish model, which was established in 1989, is the most successful deceased-donor organ donation program. The success of the Spanish model is not due to passing presumed consent law in Spain, because relatives of all potential donors must be approached and they can refuse organ donation. The success and the uniqueness of the Spanish model is its realistic approach of providing hospitals with specific budgets for organ donation and mandating the placement of trained staff who are responsible for the donation process (45).

Most of these staff are physicians, mainly intensive care unit specialists, and they belong to the staff of the hospital. They generally continue in their medical role, but as transplant coordinators, their main objective is to improve the organ donation rate. There also is increasing attention to enhance public education about organ donation. Since 1989, the Spanish model has increased dramatically the number of organ donors. This model has been so effective that the organ donation rate has increased by >100% in 10 yr (46). However, the Spanish model has not eliminated or alleviated renal transplant waiting lists.

As a result of the severe shortage of transplantable kidneys, some transplant centers now are performing ABO-incompatible living-donor renal transplants. This type of renal transplantation is costly, limited in number, and associated with more acute rejection episodes compared with ABO-compatible renal transplants (47).

Some transplant centers also are accepting volunteering altruistic strangers who are willing to donate a kidney to anyone who is in need. The large experience with a nondirected kidney donor program belongs to the University of Minnesota group. From 1997 to 2003, they received calls from 362 individuals for kidney donation. After a careful evaluation, only 23 (6%) finally were accepted and donated kidneys (48). In most developed countries, several of these strategies are being used to increase the kidney donor pool, but in none of these countries have renal transplant waiting lists been eliminated.

Currently, much of the research activities are focused, and funding is spent on xenotransplantation, genetic engineering of organs, and human embryonic stem cell studies that all have the potential to revolutionize organ transplantation by making a sufficient number of transplantable organs available. Unfortunately, none of these approaches is expected to be applicable in clinical transplantation in the upcoming decade. Until that time, the adoption of some regulated models of paid organ donation similar to the Iranian model can eliminate successfully renal transplant waiting lists and save many lives.

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