Living Unrelated (Commercial) Renal Transplantation in Children

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Abstract. Long waiting times for cadaveric renal transplantation has led the frustrated parents of Arab children with end-stage renal disease treated in our center to seek commercial renal transplantation (CRT) outside Israel. During the past 3 yr, 18 children, aged 13 ± 1 yr, underwent CRT in one center in Iraq. Post-CRT follow-up was 20.2 ± 2.5 mo. Immediate complications (abroad) included: death on the day of surgery (n = 1) and vascular thrombotic events requiring removal of a previously functioning graft (n = 2). There was a high incidence of urologic problems, mainly as a result of inadequate uretero-vesical anastomosis. Calculated creatinine clearance at 6, 12, 18, 24, and 30 mo was 84.7 ± 6.4, 91.0 ± 6.8, 90.8 ± 6.2, 82.5 ± 9.5, and 77.7 ± 8.2 ml/min per 1.73 m² respectively, representing excellent graft function in 13 patients and slightly compromised function in two children. One- and two-year patient survival was 94.4%, with a graft survival of 83.3%. CRT in these Arab children had a favorable outcome despite severe early postoperative complications. Graft function at follow-up was comparable to cadaveric renal transplantation in Israel. This may reflect a propensity for healthy young adult donors. Despite these results, the authors oppose and discourage the practice of CRT on legal and ethical grounds. Not to provide follow-up care in this specific group of patients would not have been in their best interest. (J Am Soc Nephrol 9: 1100–1103, 1998)

Kidney transplantation is the ultimate goal in treating children with end-stage renal disease (ESRD). A shortage of cadaveric kidneys and the growth in the number of dialysis patients have resulted in long waiting times for renal transplantation. This situation puts a significant medical and emotional burden on the sick children and their families. As a result, frustrated parents of Arab children who live in the West Bank and are treated in our center have looked for ways to obtain living unrelated (commercial) transplantation (CRT) in the Arab world outside Israel. Unrelated living donor (LUD) kidney transplantation in developed countries usually refers to organs received from distant relatives or emotionally related donors and has become an acceptable mode of treatment. In these countries CRT is considered unethical and illegal. This also applies to Israel.

This article is the first to address the marketing of kidneys between children with ESRD, receiving dialysis therapy, and unrelated individuals with no prior common interests. Two main issues are discussed: the outcome of transplantation and some of the ethical and legal implications of CRT in children.

Materials and Methods

Patients

Eighteen Arab children (nine boys and nine girls) living in the West Bank underwent CRT in one medical center in Baghdad, Iraq, during the years 1993 to 1996. They all received renal replacement therapy (chronic peritoneal or hemodialysis) before CRT in our center and were on the Israeli waiting list for cadaveric kidney transplantation with the same priority as all other registered young patients. The mean time period on dialysis before CRT was 2.75 ± 0.67 yr (range, 0.08 to 9.42). One-third of these children had been on dialysis for more than 5 yr before undergoing renal transplantation. The decision to travel to Iraq for CRT was made by the parents. Scheduling the hospitalization and organizing the trip was the exclusive responsibility of the family. We provided the children with a detailed medical summary. The mean age of the 18 patients at the time of their first transplantation was 13.0 ± 1.0 yr (range, 6.0 to 19.0), and the mean duration of follow-up after transplantation was 20.2 ± 2.5 mo (range, 3.0 to 36.0). The etiologic causes of ESRD in this group of patients is a good representation of the major diagnoses leading to ESRD in our entire pediatric patient population. They include dysplastic kidneys (n = 2), reflux nephropathy (n = 3), hemolytic uremic syndrome (n = 2), rapidly progressive glomerulonephritis (n = 2), focal segmental glomerulosclerosis (n = 3), and nephronophthisis, Alport's syndrome, and autosomal recessive polycystic kidney disease (n = 1, each). Three patients had ESRD of unknown etiology. The children were discharged from the hospital in Baghdad 7 to 10 d after surgery and immediately started their return journey, via Amman, Jordan, by public transportation. The patients generally arrived at our hospital without prior notification with a short standardized discharge summary. No information was provided regarding the kidney donors or the initial therapeutic regimen used to induce a state of immunosuppression. We do know that the donors were selected on the basis of a common blood group and a negative cross match but no HLA typing was performed. They all initially received a combination of cyclosporin A and oral steroids. After arrival in Israel, azathioprine was added to this regimen to provide the standard triple immunosuppressive therapy. Graft function was estimated by calculating creatinine clearance using Schwartz's formula (1) and was based on steady-state serum creatinine levels and height in centimeters. This was often
confirmed by measuring creatinine clearance on the basis of a 24-h urine collection.

A group of 17 children, matched for age at the time of transplantation, gender, dialysis time, and causes of ESRD, who underwent their first cadaveric kidney (CAD) transplantation in Israel during the same time period, was used for comparison of outcome.

**Statistical Analysis**

The data are presented as mean ± SEM. The paired t test was used to compare outcome between the two groups.

**Results**

We describe a group of patients who underwent a primary renal transplantation that was performed in one medical center in Iraq.

**Graft Function**

The graft function over the entire period of follow-up in this group of children undergoing CRT was compared with young patients undergoing cadaveric donor transplantation. In children surviving the immediate postoperative period abroad, the outcome of renal function was favorable despite excessive early complications often endangering their lives. The mean creatinine clearance rates in children undergoing CRT 6, 12, 18, 24, and 30 mo after transplantation were 84.7 ± 6.4, 91.0 ± 6.8, 90.8 ± 6.2, 82.5 ± 9.5, and 77.7 ± 8.2 ml/min per 1.73 m², respectively (Figure 1). These data are comparable to the graft function in children undergoing CAD transplantation (77.2 ± 6.0, 78.2 ± 7.9, 76.5 ± 8.0, 60.5 ± 9.9, and 69.2 ± 10.7, respectively; P > 0.05). Figure 1 clearly demonstrates a trend for superior results in those undergoing living unrelated kidney transplantation, but statistical significance was not reached due to the small number of individuals in each group. When we compared the percentage of patients in both groups with compromised graft function, defined as creatinine clearance < 70 ml/min per 1.73 m², a similar trend was noted. In the CRT group, only 23, 17, 11, 17, and 20% of children had decreased graft function at 6, 12, 18, 24, and 30 mo posttransplantation, respectively, compared with 41, 40, 30, 40, and 37.5% in those undergoing cadaveric renal transplantation.

The 1- and 2-yr patient survival was 94.4%, and the corresponding graft survival was 83.3% in children undergoing CRT, compared with 100 and 94%, respectively, in children undergoing cadaver donor kidney transplantation in our unit.

**Complications**

Children undergoing CRT had many more complications compared with the group of patients receiving CAD transplantation. The complications occurring in children undergoing CRT were arbitrarily divided into three temporal categories: immediate (occurring abroad within 2 wk of CRT), early (within 6 wk of return to Israel), and long-term.

**Immediate Complications.** One girl died on the day of surgery of causes unknown to us. Two children had acute vascular thrombotic events requiring the removal of a previously functioning graft 7 to 10 d after transplantation. After returning home, they continued dialysis treatment in our unit.

The remaining 15 children and adolescents returned to our center and all required immediate hospitalization. This was probably a reflection of the short duration of their postoperative care abroad. Several of the CRT patients were exhausted and dehydrated after a long car ride (±900 km) in a hot climate.

**Early Complications.** The most common complication in this category was hypertension, which occurred in 13 individuals and resulted in hypertensive encephalopathy in three patients. The latter was usually manifested by severe headache and generalized seizures. One patient experienced deep venous

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**Figure 1.** Renal graft function in a group of patients undergoing commercial renal transplantation (CRT) compared with children receiving cadaveric donor renal grafts (CAD). Creatinine clearance rate was estimated according to Schwartz's formula and confirmed with a 24-h urine collection. ■, patients undergoing CRT; ■, patients undergoing cadaver donor transplantation.
thrombosis that responded favorably to anticoagulant therapy, and three children had an episode of acute graft rejection with complete resolution after administration of methylprednisolone.

Long-Term Complications. We encountered a high incidence of urologic problems, mainly as a result of inadequate uretero-vesical anastomoses. This resulted in hydronephrosis in six children and led to deteriorating graft function in three that only resolved after surgical intervention. Urinary leak from the uretero-vesical anastomosis was detected in one patient but conservative management resulted in complete resolution. Eleven individuals had at least one episode of acute pyelonephritis that responded to antibiotic therapy administered intravenously. Patients who suffered repeated bouts of pyelonephritis underwent voiding cysto-urethrography, but no vesico-ureteral reflux was documented. None of the children contracted either the hepatitis B or C virus or HIV.

Discussion
The ultimate goal in treating children with ESRD requiring replacement therapy remains successful kidney transplantation. This enables adequate growth and development and allows patients and their families to lead a relatively normal life. The major obstacle in achieving this goal is the shortage of cadaveric organs and the increasing number of children awaiting kidney transplantation. On average, a child in our center has to wait almost 3 yr for a cadaveric graft. In the present article, we describe the fate of 18 Arab children from the West Bank receiving renal replacement therapy for ESRD in our center who underwent CRT. The controversial decision made by their parents to travel to Iraq for CRT was motivated by frustration with the seemingly endless suffering on dialysis and the hope of ending this suffering by purchasing an organ abroad at a reasonable price.

Two large studies in adults have recently shown that the results of living unrelated kidney transplantation are equal or even superior to cadaveric renal transplantation (2,3). Patient survival in 165 LUD kidney recipients from Brazil was similar to that in mismatched living related donor (LRD) and cadaveric donor recipients. Recipients of LUD and mismatched LRD kidneys had a better graft survival than cadaveric donor kidney recipients (74 and 76% compared with 68% at 2 yr) (2). A similar pattern has been shown in data derived from the United Network for Organ Sharing Renal Transplant Registry (United States). The 3-yr graft survival rates were 85% for kidneys transplanted between spouses, 82% for kidneys derived from parents, and only 70% for cadaveric kidneys (3). Our results demonstrate a similar pattern with a comparable and possibly slightly better graft survival for CRT compared with CAD kidney transplantation. The overall graft survival in our patients undergoing CRT seems to be similar to those receiving LRD grafts and superior to the ones receiving CAD transplantation as described in the 1995 annual report of the North American Pediatric Renal Transplant Cooperative Study (4). One- and two-year graft survival in our CRT patients was 83.3% compared with 90.5 and 86.5%, respectively, for recipients of LRD grafts and 78.2 and 72.2% for CAD graft recipients. We propose that the main factor responsible for good graft survival is the propensity to select healthy young adult donors. In addition, the ischemic damage that often occurs in cadaveric grafts before their removal is eliminated with living donor transplantation. This may lead to reduced nephron mass, resulting in increased workload of the remaining nephrons and a gradual decline in graft function (5). Because we lack information regarding HLA typing of the donors, we cannot assess this potential contributing factor. It is unlikely, however, that there is better matching in LUD transplantation.

Many of the children undergoing CRT have experienced a high incidence of urologic complications. A similar pattern has been reported in a group of adult patients who underwent CRT in Iraq and are followed in Jerusalem (6). We do not have a good explanation for this phenomenon, although it is obviously not due to lack of experience, because the Iraqi hospital performs renal transplantations almost daily.

Living organ transplantation, regardless of its motivation, should be recognized as an ethical compromise to the principle of nonmalefaseance (doing no harm), given that the donor's health is put at risk (7). Therefore, the importance of voluntary consent and the free will of the donor cannot be overemphasized. Voluntary consent is mandatory to protect potential donors from undue coercion and financial inducements. Because there is a communication barrier between the transplanting team in Iraq and our unit, we cannot be sure that these guidelines were implemented. However, from the patients and moreso from their parents, we do know that the donors were all free young adults most of whom became acquainted with the future recipients and their accompanying relatives, a pattern that is compatible with voluntary consent. In view of recent reports, it should be emphasized that we are sure that the kidneys were not obtained from executed prisoners. Our sources indicate that local regulations mandate that Iraqi citizens may not donate kidneys to foreigners. All of the renal organ donors in this report were therefore laborers from neighboring countries. Their only motivation for kidney donation is to significantly improve their standard of living. The average monthly salary of these workers seems to be $3 to $5, whereas the sum they receive for a kidney is $800 to $1000, which is equivalent to 13 to 16 yr of hard labor. For example, one kidney donor was reported to be able to abandon hard manual labor to become the proud owner of a luxurious taxicab.

The World Health Assembly endorsed a series of guidelines on human organ transplantation (8). It advocates that living donors should be genetically related, but adds that exceptions may be made for bone marrow or other regenerative tissue donations. Although it states that the human body and its parts cannot be the subject of commercial transactions, it leaves the method of implementation, including possible sanctions, to the discretion of local authorities. Furthermore, it does not prohibit "rewarded gifting," namely, payment of reasonable expenses to the donors.

If exploitation of donors is avoided and the role of brokers is omitted, it may be claimed that kidney donation is a gift of life and that financial incentives are therefore morally justified (9--11). This issue was further debated by Brecher, who
claimed that selling a kidney is not a crime and if anybody is to be blamed at all, it is the customer, because buying an organ is a form of exploitation based on making a commodity of the human body (12).

These issues become even more complicated when the suffering and ultimately the lives of children are at stake and not the "customers," but their legal guardians, are the decision-makers. In this situation, one has to weigh what society has deemed ethically wrong against the individual rights and needs of the specific patient. Indeed, we felt uneasy with the attitude of parents who were willing to buy an organ without giving serious consideration to the possibility of donating a kidney to their own sick children. The question of financial incentives for living donors should be decided by local communities, and include lawmakers, medical professionals, moralists, patients, and the public. The attitude toward financial incentives for the families of potential cadaveric kidney donors was addressed in a survey conducted among adult dialysis patients. This recent report showed that although dialysis patients are likely to benefit from the increased supply of kidneys, many would still prefer altruistic motives as the main incentive to organ donation, even if this means fewer kidneys (13).

We were confronted with the ethical dilemma of providing immediate medical follow-up care to children who underwent CRT. Because the transplantation and all of the accompanying transactions were performed outside our country and beyond our jurisdiction, we felt that we had no legal liability. Furthermore, the patients live in the West Bank, where Palestinian authority rules and we have no legal say. We were also very careful to explain to the parents that CRT is not an accepted form of treatment in Israel and most Western countries. According to British law, our actions may even have involved a charge of being an accessory to a crime (14).

In the problematic situation we confronted, we felt that the children were blameless. There are no pediatric nephrologists with dialysis facilities in the entire West Bank, which has an estimated population of 1.75 million. Denying medical care would have probably resulted in more suffering and even death for these children, and in the final analysis this had to be our only ethical consideration.

References