Pediatr Nephrol (2008) 23:1925–1929
DOI 10.1007/s00467-008-0858-2

EDITORIAL COMMENTARY

Trends in unrelated-donor kidney transplantation in the developing world

Rashad S. Barsoum

Received: 5 January 2008 / Revised: 22 February 2008 / Accepted: 4 April 2008 / Published online: 7 June 2008

Abstract Living unrelated donors (LUDs) constitute an incremental source of kidneys for transplantation at a global level. Excellent outcomes are reported, superior to those of deceased-donor transplantation and comparable to related donor transplantation. LUD include six categories: spouses, distant relatives, paired-exchange, living-deceased exchange, and non-directed and directed donors. Although a financial reward may be involved in any of these categories, it is in the declared selling of organs that ethical concerns have intensified. There are three patterns of paid LUDs in the developing world: organized, erratic and commercial. The only model of organized LUDs is in Iran, where a central agency assigns and compensates the donors. Erratic LUD transplantation has been experienced, and subsequently banned, in the development of transplant programmes in most developing countries. However, the tightness and enforcement of the official ban are geographically different, providing variable room for uncontrolled trafficking. Commercial transplantation has, thus, become phenomenal in a few countries, gradually evolving into an organized business that follows market dynamics, including advertisement, brokerage, commissions, auctions and tourism. While most international organizations and activist groups condemn commercial transplantation, it is often perceived, in certain cultures and under particular socio-economic standards, as a human right that meets the demands of all stakeholders, and should be organized rather than declined just for the purpose of meeting the values of a third party.

Keywords Transplant tourism · Unrelated living donors · Directed living donors · Undirected living donors · Organ trafficking

R. S. Barsoum
Kasr-El-Aini Medical School, Cairo University,
Cairo Kidney Center,
Cairo, Egypt

R. S. Barsoum (✉)
Cairo Kidney Center,
3 Hussein El-Memar Street, Kasr-El-Nile, P.O.B. 91,
Bab-El-Louk, Cairo 11513, Egypt
e-mail: rashad.barsoum@gmail.com

Introduction

The practice of kidney transplantation has never been short of motivation, being the ultimate goal of the typical stakeholders involved in the management of end-stage renal disease (ESRD). Compared with dialysis, transplantation has gracefully offered to the patients prolonged survival and improved quality of life; to the medical profession, better knowledge and pride; to the health sponsors, a better cost-effective solution for an aching problem; and to the community, pragmatic relief from a high-impact socioeconomic burden.

Yet the bottle neck that checks its potential in any transplant programme is the unavailability of enough donors. Regardless of many logistic, ethical and biological debates, the pool of unrelated donors has globally expanded at a much faster rate than that of live-related and deceased donors [1, 2] (Figs. 1 and 2).

Outcomes of living unrelated-donor transplantation

Beyond ethical debates, unrelated-donor organ transplantation has certainly provided valuable scientific and clinical information. The outcome of such transplantations was a

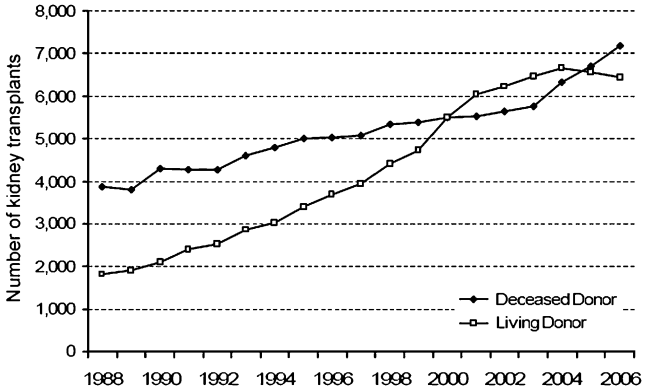

Fig. 1 Relative growth of living- and deceased-donor kidney transplants in the USA in 12 years (United Network for Organ Sharing data) [1]

matter of strong disagreement during the 1990s. While the Brazilian [3], Iranian [4] and Egyptian [5] experiences claimed excellent outcomes, superior to those in cadaver and close to living related-donor transplants, there were contradictory reports in several studies [6, 7]. Careful analysis suggests that the difference was, indeed, related to a "centre effect". Most of the poor outcomes of living unrelated-donor (LUD) transplantations were attributed to poor standards of medical care in commercial transplant programmes, infections transmitted with the donor organs, or patient non-compliance. Most subsequent reports, correcting for these factors [8], including that in the present issue of *Pediatric Nephrology* [9], have shown no significant difference in the intermediate-range patient or graft outcomes compared to those in living related transplants. This observation supports the concept that the role of tissue mismatching is less significant than the potent effect of modern immunosuppressive protocols. Consequently, the relatively inferior outcomes of deceased-donor organ transplants must be attributed to non-immunological factors, such as the death-associated cytokine storm, perfusion, storage, ischaemia and reperfusion injury.

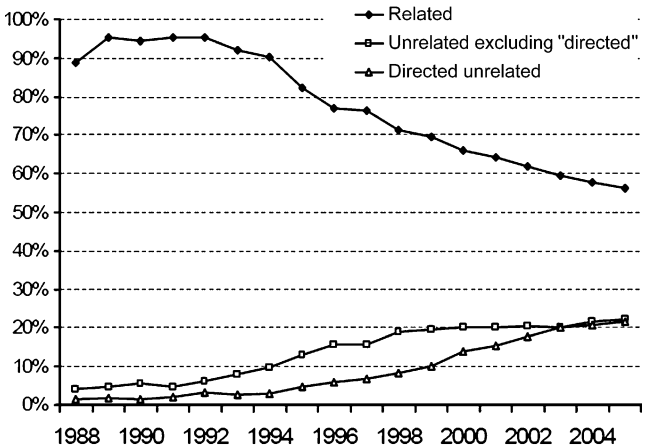

Fig. 2 Proportional contribution of related, undirected and directed kidney donors in the USA (United States Renal Data System) [2]

There are no controlled studies comparing, head-to head, the long-term outcomes of transplantation from live-related donors versus unrelated donors. However, registry data suggest a trend towards better survival of unrelated donor kidneys (Fig. 3), unconnected to tissue types [10]. This suggests that the non-immunological components of chronic allograft nephropathy, such as calcineurin inhibitor nephrotoxicity, graft arteriosclerosis, viral infections, and recurrence of glomerulonephritis, are masking the effect of histocompatibility mismatching.

Global profile of LUD transplantation

Unrelated donors may be classified into six categories, namely spouses, distant relatives, paired-exchange, living–deceased exchange, non-directed (no specific recipient identified) and directed (intended for a particular individual) [11]. While all classes are more or less accepted on ethical grounds, there is considerable concern that the bottom line in most LUD transplantations may involve a material benefit to the donor, thereby violating time-honoured medical values as well as the international law [12]. In the cumulative world experience, some of the most unfair financial agreements were covered by apparently pure altruistic motives. There are documented records of pre-transplantation marriage–divorce agreements for money, false allegations of distant family relationship among strangers, "undirected" humanitarian donations turning out to be a hidden call for a higher bid, etc. It would be naive to exclude a donor–recipient financial arrangement in frankly "directed" LUD transplants, regardless of any statements or signed consents to the contrary. From time to time, one even stumbles on a discrete financial agreement between siblings or closely related donor–recipient pairs, which

Fig. 3 Graft survival of inter-spouse kidney transplants compared to other live donors, including related donors (Collaborative Transplant Study Group data, K-15301–0807) [10]

speaks of the dominance of pragmatic benefit exchange in the act of organ donation.

For the sake of accuracy, I shall focus only on the declared paid donors, regardless of their categorization, and on one organ, the kidney. This practice may be arbitrarily classified into three patterns, namely the "organized", regulated through a national plan; the "erratic", where LUD donation is an accepted, partially controlled practice; and the "commercial", where transplantation is a recognised business subject to market rather than ethical rules.

Organized live-unrelated donation

The only model in this category is in Iran. The whole process is centrally organised by an official non-profit organisation, equivalent to the National Kidney Foundation, called "Dialysis and Transplant Patients Association (DATPA)", members of which are patients with renal failure [13]. DATPA undertakes the task of assigning suitable donors for referred recipients and provides medico-legal coverage. Donors receive finite financial compensation from the government and non-profit organisations, through DATPA, plus free life-long health insurance and, often, a "rewarding gift from the recipient" [13]. This model has worked very well over two decades, completely eliminating the transplant waiting list and providing the gift of life to about 10,000 patients with ESRD, comprising over three-quarters of the overall kidney transplant activity in the country. Interestingly, this trend continued even after a deceased-donor programme was developed in 2000.

Several authorities on medical ethics tend to see the Iranian model as being a fair compromise, which solves many regional logistic problems for both recipients and donors and avoids such ugly experiences as transplant commercialism and tourism [14]. On the other hand, although LUD safety in terms of physical morbidity and long-term survival has been documented in many studies [15, 16], the extensive Iranian experience has shown significantly negative subjective effects on donors' quality of life for up to 11 years after donation [17]. Depression and anxiety were predominant features in over 70% of 300 donors addressed by the RAND SF-36 questionnaire, which may explain their ill-defined functional complaints. Depression was largely situational, being attributed to social rejection by family, spouses and their own recipients. Over 80% ended up in worse economic standing, presumably due to inadequate management of their financial reward. Similar observations were made in other cohorts, including a recently published report of Egyptian LUDs [18]. On the other hand, a study in the latter country showed that donor depression preceded donation, again attributed to their pressing socioeconomic problems [19].

Erratic live-unrelated donation

This generally occurs in countries where deceased-donor organs are not available for different reasons, such as the long waiting lists in several industrialised countries (e.g. the USA) [2] (Fig. 2) or the lack of legislation for the use of cadaver organs in many developing countries (e.g. Egypt).

The Egyptian experience is essentially driven by the lack of any formal legislation for organ transplantation and, subsequently, cadaver donor transplants. In 1979, only 3 years after the first live related-donor transplantation, the team at Cairo University accepted the reasoning of a nurse wishing to donate a kidney to her team's physician. This opened the door for other "emotionally related", donors, which gradually expanded to encompass different motives, including the donor's financial shortage.

While the expanding pool of unrelated donors has met the interest of all stakeholders, it resulted in a chain of negative effects. By offering an alternative, it damped the willingness of immediate family members to donate, as well as the public enthusiasm for setting the scene for a cadaver donor programme. Since the demand remained higher than supply, the "compensation" claimed by the donors increased beyond the average paying ability of the average Egyptian, which ultimately recruited patients from neighbouring rich countries to compete for a piece of the cake. Thus, a market was created, following all the market rules and tools, including the emergence of brokers, auctions, commissions, and so on.

In 1992 members of the Egyptian Society of Nephrology, driven by national pride and professional dignity, voluntarily decided to abandon all unrelated-donor transplantation. This attitude was supported by the Egyptian Medical Syndicate and emphasised by strong local and international [20] media propaganda. It resulted in a modest decline in the number of transplant operations performed in the country by about 20% during the following year [21], yet with a significant change in the related/unrelated donor profile, as shown in Fig. 4.

However, since the ban did not have the power of law, it was only partially honoured and did not last long. The rapidly growing demand became a political issue, and the expense of covering the national dialysis programme became insurmountable. Eventually, the Minister of Health exempted the State hospitals from this ban, and, in response, the Egyptian Medical Syndicate eased the regulations by accepting unrelated donors for recipients of the same nationality, only after obtaining official clearance by a central ethics committee that included only one conflict-free nephrologist for technical advice.

The Syndicate's clearance ensured transparency, relieved the transplant teams of some of their ethical burden and conferred professional support pending adequate legislation.

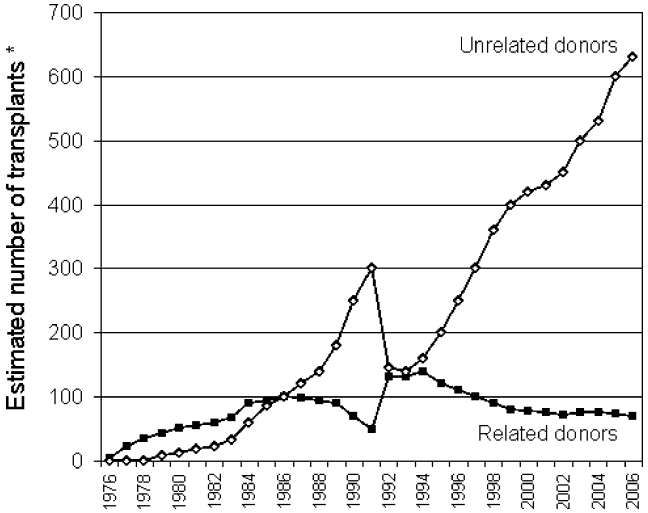

Fig. 4 Growth of related and unrelated donor kidney transplantation in Egypt in 30 years. *Numbers were estimated from different sources, including government reports, Egyptian Society of Nephrology, publications and personal communication

The Syndicate's role extended beyond granting permission; to explaining the risks and consequences and obtaining the donor's informed consent. However, it was clear that, when it came to facing criminal accusation of inflicting injury on the donor, the syndicate's clearance would not provide legal defence of any value. For this reason, most transplant centres developed their own ethics committees and obtained additional consent, in order to confer institutional rather than team legal responsibility on LUD transplantation.

Location of a suitable donor became the function of tissue typing laboratories, whose role gradually shifted from individual pair matching to exchange of donors recruited by different recipients for the sake of best matching, and finally to act as "live donors' banks".

This formula was palatable to all stakeholders, being seen as fairly controlled, maintaining national dignity, and avoiding a lot of institutional bias, embarrassment and part of the legal responsibility. However, the ethical debate on the concept of "selling organs" continues. On one hand are those who believe in the values of human dignity, completely condemning the core concept of donation for money. On the other are the pragmatic defenders of "human rights" of a sane adult to do whatever he/she wishes with his/her body, so long as no evil is done to the community, as well as his/her right to be compensated for this deed. In essence, the debate looks like one in between community image and individual freedom. From many donors' perspective, the community is providing too little social support to claim any right of prioritising its image at the expense of their suffering from poverty and lack of even the minimal satisfaction of essential family needs.

While the Egyptian, partly controlled, organ-trafficking practice continues, it is unfortunate that a few members of the profession breached the Syndicate's order, by illegally performing transplantations from Egyptian-donors to non-Egyptian recipients. The size of this "market" is impossible to measure, though a recent undocumented study estimates it as 100–400 transplant operations per year [22].

This story repeats itself in many developing countries. Yet, there are differences in the level to which the scenario has progressed. Some countries still indulge in the pool of commercial transplantation (e.g. China, about 2,000 cases/year; Pakistan, 1,000–1,500; the Philippines, 100–200; Colombia, about 70 [17]). Others continue erratic LUD transplantation, with variable restrictions (e.g. India, fewer than 50 tourists in 3,000–4,000 transplant operations), and a few seem to continue following the ban, trying completely to replace live-unrelated donors with cadaver donors (e.g. Brazil).

Commercial live-unrelated donation

This is pure business. The motives of transplantation are clearly announced as such in different media, including the Internet [23], and the set-up is geared as any other business. Recipients are recruited to transplant centres as individuals or groups, donors by brokers, and the whole business is overseen by financial and legal experts. The same ethical debate between community image and personal freedom applies, with even stronger stands of both opponents. The World Health Organisation has issued a strong resolution condemning organ trafficking [24], which is supported by other international bodies such as The Transplantation Society (TTS). Several activist groups have been formed to combat this practice and to protect the donors' rights in non-commercial LUD transplantation [18, 25]. Francis Delmonico, who has been a driving force in protecting living donors' rights [25], has been instrumental in changing the ugly image of commercial transplantation in many parts of the world, including China and the Middle East. Whether these achievements will be sustained against the will, blessing and counter-argument [26] of directly involved stakeholders remains to be seen.

Conclusion

There is no ideal solution to this global dilemma. As in many other areas in medicine, technical advancement continues to pose organisational challenges, usually financial and frequently ethical. Both factors are highly dominant in the developing world. The financial shortage and lack of a fair social security system is the main reason for the selling of organs, while the income gradient between the industrialised and developing world is the driving force for trafficking and transplant tourism. The ethical challenge

is a composite mix of religion, culture and compromised public education. Accordingly, debate on issues such as brain death or donor compensation is often emotional rather than rational, which echoes as legislation delay. Where the law is indecisive, the door is open to personal bias and chaotic practice. It is clear that major organisational progress can be achieved by enforcing legislation on the basis of country-specific factors. It would be a mistake if a universal rule is believed to work under such diverse economic and cultural conditions as they are in the developing world.

References

1. United Network for Organ Sharing (UNOS). National data/ Donors. http://www.optn.org/latestData/step2.asp. Accessed 27 December 2007
2. United States Renal Data System (USRDS). Transplantation/By donor type. http://www.usrds.org/adr.htm. Accessed 27 December 2007
3. Sesso R, Josephson MA, Ancao MS, Draibe SA, Sigulem D (1998) A retrospective study of kidney transplant recipients from living unrelated donors. J Am Soc Nephrol 9:684–691
4. Ghods AJ (2002) Renal transplantation in Iran. Nephrol Dial Transplant 17:222–228
5. Barsoum R, Bakr MA (2000) The Egyptian renal transplant experience. Clin Transpl 2000:359–360
6. Sever MS, Kazancioğlu R, Yildiz A, Türkmen A, Ecder T, Kayacan SM, Celik V, Sahin S, Aydin AE, Eldegez U, Ark E (2001) Outcome of living unrelated (commercial) renal transplantation. Kidney Int 60:1477–1483
7. Jha V, Chugh K (2006) The case against a regulated system of living kidney sales. Nat Clin Pract Nephrol 2:466–467
8. Terasaki P, Cecka JM, Gjertson DW, Takemoto S (1995) High survival rates of kidney transplants from spousal and living unrelated donors. N Engl J Med 333:333–336
9. Gheith O, Sabry A, Abd El-Baset S, Hassan N, Sheashaa H, Bahgat S, El-Shahawy E (2008) Study the effect of donor source on graft and patient survival in pediatric renal transplant recipients. Pediatr Nephrol DOI 10.1007/s00467–008–0760-y
10. Collaborative Transplant Study. Relationship unrelated living donors, first kidney transplants 1991–2005. http://www.ctstransplant.org/protected/dataR/html_all/ K-15301–0807.html. Accessed 27 December 2007
11. Davis CL, Delmonico FL (2005) Living-donor kidney transplantation: a review of the current practices for the live donor. J Am Soc Nephrol 16:2098–2110
12. Delmonico FL (2007) Organ trafficking and transplant tourism. NATCO 32nd Annual Meeting New York. http://www.natco1.org/members/NATCO2007AnnualMeeting.htm. Accessed 27 December 2007
13. Ghods AJ, Savaj S (2006) Iranian model of paid and regulated living-unrelated kidney donation. Clin J Am Soc Nephrol 1:1136–1145
14. Daar A (2006) The case for a regulated system of living kidney sales. Nat Clin Pract Nephrol 2:600–601
15. Fehrman-Ekholm I, Elinder CG, Stenbeck M, Tydén G, Groth CG (1997) Kidney donors live longer. Transplantation 64:976–978
16. Matas AJ, Bartlett ST, Leichtman AB, Delmonico FL (2003) Morbidity and mortality after living kidney donation, 1999–2001: survey of United States transplant centers. Am J Transplant 3:830–834
17. Zargooshi J (2001) Quality of life of Iranian kidney "donors". J Urol 166:1790–1799
18. Coalition for Organ Failure Solutions. http://www.cofs.org/egypt.htm. Accessed 27 December 2007
19. Farid M, Torky H, Barsoum R (1996) Related and unrelated live kidney donors: social and psychological analysis. Med J Cairo Univ 64:251–257
20. Hedges C (1992) Egyptian doctors limit kidney transplant. New York Times, 23 January 1992
21. Barsoum R (1992) The Egyptian transplant experience. Transplant Proc 24:2417–2420
22. Shimazono Y (2007) 2nd WHO global consultation on human transplantation. Geneva, pp 28–30
23. Shimazono Y (2007) The state of the international organ trade: a provisional picture based on integration of available information. Bull World Health Organ 85:955–962
24. Resolution on human organ and tissue transplantation (2004) Geneva: WHO; (WHA57.18). Available at: http://www.who.int/transplantation/en/A57_R18-en.pdf
25. Delmonico FL (2006) What is the system failure? Kidney Int 69:954–955
26. Matas A (2006) Live kidney organ donation: is it time for a different approach? Why we should develop a regulated system of kidney sales: a call for action. Clin J Am Soc Nephrol 1:1129–1132