

## Living Kidney Donation: Evolution of Strategies

Editorial

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Renal transplantation (RT) represents the best therapeutic option for patients with end-stage renal disease (ESRD), providing the best outcomes for survival, quality of life, and cost-effectiveness [1]. The widening gap between the recipients waiting for RT and the number of available kidney donors has led to annual expansion of the waiting list and dramatic increase in the morbidity and mortality due to the long waiting times for patients on dialysis. The living kidney donation (LKD) has become increasingly important in recent years due to decrease in the number of deceased kidney donors. There has been significant increase in the number of LKD over past decade due to enhancement of the education of the donors and recipients about LKD, introduction of minimally invasive surgical techniques of donor nephrectomy, expanded criteria for donor acceptance, informed consents, rigorous follow-up regimens, blood group ABO-incompatible (ABOi) and positive cross-match transplants and non-directed altruistic donations [2]. This editorial summarises the evolution of practice that has taken place over past six decades to encourage living kidney donation.

Since the first successful RT performed between the identical twins in the Peter Brent Brigham Hospital, Boston on 23<sup>rd</sup> December 1954 by Murray et al, RT has become a routine [3]. According to the World Health Organisation, in 2014, a total of 33055 living donor renal transplants (LDRT) were performed in 97 countries worldwide [4]. Living donor RT allows a planned pre-emptive transplants with better long-term outcomes compared to patients on dialysis. In addition, the LDRT has better graft function and better graft survival which is due to the predictability of the donation, the optimal conditioning of donor and recipient, and the short ischemia time [5].

For more than 60 years, living donor nephrectomy was performed through a flank incision. To remove the disincentives of open nephrectomy, Ratner et al., introduced laparoscopic donor nephrectomy (LDN) in 1995, which has gained widespread acceptance and popularity; currently all donor nephrectomies in the United States and United Kingdom are performed with this technique [6]. The advantages of LDN are reduced post-operative pain, shorter recovery period and hospital stay, early return to work and better cosmesis. Variations in the surgical techniques such as total versus hand-assisted laparoscopic and transperitoneal versus retroperitoneal, have shown similar outcomes [7, 8]. This has contributed significantly to the increased living kidney donation. The recipient outcomes after LDN are identical to those observed after open nephrectomy [9, 10].

Robotic-assisted donor nephrectomy is the recent development, which as compared to traditional laparoscopy, provides better EndoWrist instruments and three-dimensional visualization of the operative field. Studies published so far indicate that LDN using the robot-assisted technique is safe, feasible, and provides remarkable advantages for the patients. From a systematic review including 5 papers (292 patients), the complications rates and outcomes were similar to those of conventional LDN [11].

Although the donors are thoroughly assessed prior to donation, the complications after donation raises concerns among the donors. A US study of transplant registry including 97 centres, identified the pre-donation comorbidity and perioperative complications among 14964 living kidney donors, where nephrectomies were predominantly laparoscopic (93.8%); 2.4% were robotic and 3.7% were planned open procedures. Overall, 16.8% of donors experienced a perioperative complication; such as gastrointestinal (4.4%), bleeding (3.0%), respiratory (2.5%) and surgical/anaesthesia-related injuries (2.4%). Obesity (OR 1.55,  $p = 0.0005$ ), pre-donation hematologic (OR 2.78,  $p = 0.0002$ ) and psychiatric (OR 1.45,  $p = 0.04$ ) conditions were associated with increased risk of complications [12]. One hundred kidney transplant physicians and surgeons from 40 countries from the world met in Amsterdam, April 1-4, 2004 and have drafted guidelines on the Care of the Live Kidney Donors, which has been adopted for the evaluation of the donors [13].

To alleviate the shortage of kidney donors, several advances have been made to improve the utilization of donors deemed incompatible with their intended recipients who are ABOi and antibody-incompatible due to sensitisation. The most prominent of these advances is kidney paired donation, which matches incompatible patient-donor pairs to facilitate a kidney exchange [14]. In 1987, Alexandre et al. introduced an effective desensitization protocol to achieve success in ABOi living donor RT [15]. This protocol included pre-transplant repeated plasmapheresis as a strategy not only to reduce the titres of anti-A or -B antibodies, but also to decrease the anti-lymphocyte globulin-based induction. A one-year graft survival of 75% and a recipient survival of 88% were achieved in the 23 recipients [16, 17]. Although patients with moderate titres of anti-A/B antibodies may easily be desensitised with no negative impact on allograft survival, recipients with high titres and HLA sensitized patients demonstrate a substantial risk for antibody-mediated rejection, limiting long-term outcomes [18]. Special strategies such as the Eurotransplant Acceptable Mismatch Program or kidney paired exchange help improving long-term outcomes in these difficult to transplant patients by circumventing the HLA or ABOi antibody barrier [18]. There is an increas-

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ing trend towards non-directed altruistic donation, which increased the donor pool and assisted in initiating the exchange donation chain [19].

Despite the stressful life event of donation, donors have shown high resilience and high levels of quality of life post-donation, which has been confirmed by several studies [20, 21]. Living kidney donors undergo a major operation for the benefit of others, hence informed consent process with disclosure of complications is paramount. A recent web-based survey including 50 kidney transplant surgeons in 8 transplant centres showed that bleeding was the only complication every surgeon mentioned. Risk of death was always mentioned by less than 50% surgeons and the reported mortality rates ranged from 0.003% to 0.1%. Mentioning frequencies for all other complications varied [22].

In a study published from Sweden, better survival among the living donors were reported probably due to the fact that only healthy persons are accepted for LKD [23]. However, current evidences indicate to the contrary. The prevalence of chronic kidney disease stage 3 (eGFR <60 mls/min/1.73m<sup>2</sup>) does increase post donation, particularly in elderly donors [24]. Prevalence of ESRD was 1.1%. All-cause mortality was 3.8% and all the renal deaths on average occurred 10 years post-nephrectomy [25]. In a study involving 1901 donors with a median follow-up of 15.1 years and 32,6210 potentially eligible kidney donors with a median follow-up of 24.9 years, the hazard ratio for all-cause mortality was increased to 1.30, cardiovascular death to 1.40, and ESRD to 11.30. The risks of gestational hypertension or pre-eclampsia seem to be 6% higher in pregnancies among donors than in pregnancies among healthy non-donors [26, 27].

In summary, significant success has been achieved in LKD and RT over past six decades to meet the increasing demand of organs from rising number patients with ESRD. Thorough assessment of potential donors, informed consent, availability of minimally invasive surgery, successful RT against immunological barrier and proven safety of the donation with excellent recipient outcomes have contributed to the current state of living kidney donation. A multidisciplinary approach to enhance the understanding of the LKD process among the potential donors, recipients and their families is paramount to increase the LKD further [28].

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