

Long-term outcome of living kidney donation

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Among the therapeutic options for end stage renal disease (ESRD), kidney transplantation from living donors currently represents the best treatment, giving superior results in terms of patient survival and quality of life when compared with deceased donor kidney transplantation or dialysis [1,2]. Organ shortage and limited expansion of the deceased donor pool in the last decade have multiplied demand for living kidney donation all over the world. Yearly, more than 27,000 living kidney donations are performed worldwide, accounting for almost 40% of all kidney transplants.

Living kidney donation requires a healthy volunteer to undergo nephrectomy, a procedure reported to have the extremely low perioperative mortality rate of 3.1 cases per 10,000 kidney donation procedures, which is 6 times lower than the surgical mortality reported for laparoscopic cholecystectomy [3]. However, the choice of life with a single kidney is also associated with an unavoidable degree of reduction in renal function [4].

Therefore, the European Committee on Organ Transplantation (CD-P-TO) believes that it is imperative for the transplant community to define precisely the risks associated with living donation, to identify potential living donors who are at increased risk of long term complications following kidney donation, and to communicate these shortcomings upfront and clearly to candidate donors primarily through direct doctor-patient relationship.

In all cases, the CD-P-TO emphasises that free life-long monitoring should be offered to all living donors following kidney donation. Particular consideration should be given to donors travelling from overseas to donate, especially those from developing countries, as these individuals may have limited resources or access to

health care in the longer term. In addition, the establishment of national or even supranational registries to monitor live donation and its consequences should be regarded as highly desirable [5].

To date, the risk of ESRD for living donors has been considered to be lower than, or no different to, that of the general population (180 vs 268 cases/10⁶ person-years) since living donors are thoroughly screened and reportedly healthier than controls who have had no screening [6].

However, two recent studies published in the last year where long-term risks have been analysed in large cohorts of healthy living kidney donors and compared to those of matched healthy controls, have come to challenge the conclusions of such earlier reports.

In a first study from Norway, 1,901 living kidney donors were compared to 32,621 potentially eligible kidney donors [7]. The study showed that, amongst donors there was a significantly increased long-term risk for ESRD (0.47% vs 0.067%; hazard ratio 11.38), cardiovascular, and all-cause mortality (cumulative incidence at 25 years of 18% in donors vs. 13% in controls). It should be noted, however, that in this study a considerable proportion of the living donors were on average 8 years older and had a longer follow up compared to controls, resulting in a potential age-derived bias with regard to the development of ESRD or the incidence of death in the donor group.

Moreover, all donors with ESRD (n=9) were biologically related to their recipients and the renal disease was immunologic, suggesting the possibility of a hereditary factor. In addition, the control group derived from a restricted geographic area within Norway and was selected in a survey conducted in a limited period of

time (1984-1987), raising doubts about the appropriateness of controls.

In a second study conducted in the USA, a cohort of 96,217 living kidney donors was compared with a population of 9,364 healthy-matched non-donor controls [8]. In this study, kidney donors had an increased risk of ESRD (7 times) over a median of 7.6 years, although the magnitude of the absolute risk increase was small (0.9% vs 0.14%). In this regard, however, the absolute risk for ESRD was not based on the actual number of ESRD cases recorded during the study but was the ultimate result of a complex statistical elaboration. The 15-year cumulative incidence of ESRD was higher among older donors and African-American donors. Increased incidence in the latter group could be due to either genetic factors or to increased risk of developing comorbidities after donation (e.g. hypertension). Nevertheless, when compared to the general unselected population, living donors had much lower estimated lifetime risk of ESRD (90 cases per 10,000 in living donors vs 326 cases per 10,000 in healthy matched controls, i.e. 3.6 times lower).

In summary, a higher risk of developing ESRD among kidney donors is documented in these recent studies conducted in two large cohorts of living donors compared to their matched non-donor counterparts. The chances for living donors to develop ESRD during their lifetime appear to be marginally increased (incidence lower than 1%) though the magnitude of the absolute risk increase is small and is much lower than that of the general population. In addition, the data suggest that such an increased risk may be primarily confined to African-American donors and to a selected subgroup of biologically related donors whose recipient's ESRD was the consequence of an immune-mediated process. Moreover, both these studies present several methodological shortcomings that may have contributed to a slight overestimation of the said risk.

However, the risk of developing ESRD among kidney donors evidenced by these reports cannot be hurriedly dismissed. Furthermore, the long-term mortality risk is still controversial among studies.

Prior to any intervention, living kidney donors must be given comprehensive information as to the purpose and nature of the surgery to remove a kidney, as well as on its consequences and risks, to enable the donor to give her/his informed and free consent. Therefore, based on these recent observations, the CD-P-TO believes that complete and updated information to living donors should reflect that:

- 1) Living kidney donation is the best option for ESRD in terms of patient and graft survival, and is supe-

prior to deceased-donor kidney transplantation or dialysis;

- 2) Among all types of surgical procedures, the peri-operative mortality of kidney donation is extremely rare, occurring in 3.1 per 10,000 cases, which is 6 times less than the surgical mortality for a low risk procedure such as laparoscopic cholecystectomy;
- 3) Analysis of large donor populations in North America and Europe are not conclusive in defining the possible adjunctive long-term risk of death for living kidney donors with respect to healthy-matched non-donors;
- 4) Living kidney donor candidates should be selected among the individuals who carry the lowest risk of developing ESRD in their lifetime. While two studies have shown that this risk may increase by several fold after kidney donation (7-11 fold compared with controls), the percentage of risk still remains low (0.47% vs 0.067% [7] and 0.9% vs 0.14% [8] in living donors and controls, respectively), the absolute risk being 3.6 times less than that of developing ESRD in the general population. Such a risk appears to be primarily confined to a selected portion of the donor population that includes donors who are biologically related to recipients with immune-mediated kidney disease and black donors.
- 5) Possible factors that may predict a risk of developing ESRD in the lifetime of living kidney donors include donor co-morbidities (such as obesity, hypertension and ethnic genetic association) and age at the time of nephrectomy. In this regard, it should be noted that predicting long term outcome is more difficult in younger donors compared with older donors where the assessment of residual renal function and subsequent decline over time is more predictable. Whatever the case, the possible impact of risk factors that were identified during the evaluation process must be carefully explained to the potential donor.

Based on these data, the current opinion at the CD-P-TO is that living kidney donation should continue to be considered as a safe, acceptable and effective procedure, allowing transplantation to go ahead against a background of profound shortage of organs from deceased donors. It should also be regarded as an expression of respect for the autonomy of the donor.

It is the view of the CD-P-TO that recent studies reinforce the need for life-long follow up of donors so that risk factors for ESRD that accumulate over a lifetime can be properly assessed. Health professionals and administrations should make all efforts to increase the available evidence on the risks of donating a kidney during one's lifetime to provide potential donors with the necessary

data for properly informed consent. It is only in a climate of complete trust and transparency that healthcare professionals will increase confidence in living donation.

In this light, the CD-P-TO recommends that the above information is incorporated into discussions with donors about the risks and benefits of this generous gift, and is included in the provisions of the informed consent.

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