

Ethics and living donation in renal transplantation

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ABSTRACT

Living kidney transplantation is the treatment that offers the best benefits in end-stage kidney disease, and one in which Beauchamp and Childress' ethical principles should govern proceedings.

In this review, we address the principles of beneficence, non-maleficence, autonomy and justice in living donation. Receptor and society benefits from donation are clear, and donors benefit from psychological and moral gains. Non-maleficence is respected: the intra and immediate post-operative risk of death are minimal, as are the known medium and long-term medical risks. In summary, living kidney donation is an ethically acceptable procedure, based on the four pillars of medical ethics. A clear and informed consent of both donor and receptor is essential.

Key-words: Ethics, living donation, kidney, transplantation

INTRODUCTION

The best treatment for patients with end-stage renal disease (ESRD) is renal transplantation, which has a 68% reduced risk of death compared to that of patients on the waiting list^{1,2}.

In Portugal, Law 22/2007 of 29th June³ legislates transplant practices, partially transposing European Parliament Directive n^o 2004/23/EC of 31st March⁴. Articles 68 and 69 of the Portuguese Medical Ethics Code Code reflect the deontological perspective⁵.

Nevertheless, the transplant community is dealing with organ scarcity in cadaveric transplantation, and potential receptors in Portugal spend an average of 5 years on the waiting list before receiving a kidney⁶. The following numbers illustrate this: in Portugal, in 2016, more than 7000 patients were on the waiting list for renal transplantation; only 513 patients were

transplanted, 65 of whom received a kidney from a living donor⁷.

Studies showed that dialysis time prior to transplantation, regardless of the type of donation (cadaveric or living), determines transplant outcome: preemptive transplantation has better results and those undergoing dialysis for more than two years have worse results⁸. Many will die in this waiting period. In addition to the increased risk of death, patients who remain longer on the waiting list are at a higher risk of graft loss⁸.

If we compare patient and graft survival between cadaveric and living donation, living donation is clearly superior. The 1-year unadjusted survival rates range from 95% to 98% for recipients of a deceased donor and living donor, respectively. The five-year patient survival is greatest for live donor kidney recipients (90%) than for non-extended criteria (83%) or extended criteria (69%) deceased donors recipients⁹. Better graft

survival remains the case even for unrelated living donors with six haplotype mismatches requiring desensitization protocols for recipients^{10,11}.

As a result, there is a growing implementation of programmes for kidney living donation, as established by the 15th article of Portuguese Law nº 22/2007³, dealing with the therapeutic interest of the recipient and non-available cadaveric donor.

However, kidney living donation can bring about ethical dilemmas, including issues related to the Beauchamp and Childress principles, which the medical community needs to respect¹².

■ METHODS

We performed a bibliographic review of the ethical aspects addressed in living donor renal transplantation, using PubMed MEDLINE, looking into who can donate and to whom. We considered the short, medium and long-term risks from living kidney donation based on the principles of beneficence and non-maleficence; the donors' rights regarding justice and autonomy in the donation, individualizing the type of recipient and the renal disease of the potential recipient. In this review, we used sources of information in the areas of organ transplantation, nephrology, and medical ethics.

■ ETHICS AND LIVING DONATION IN RENAL TRANSPLANTATION

The principles of Beauchamp and Childress of beneficence, non-maleficence, autonomy and justice are the mainstays of medical ethics¹². These must be observed and respected in every medical evaluation of a potential donor.

■ The principles of beneficence and non-maleficence

Living kidney transplantation is indeed advantageous for the recipient whether by increasing survival (of both recipient and graft), or by increasing the quality of life. Living kidney transplantation is also a benefit to society since it provides a cheaper alternative therapy after the 3rd year of transplantation¹³. To the donor, the benefit will be psychological and moral^{14,15}.

Is it ethical to expose a healthy person to risks for the benefit of another person?

The good outcomes in kidney living donation are allied with screening for significant health conditions associated with kidney disease at the time of the transplant. The European Renal Best Practice (ERBP) guidelines¹⁶ published the procedures for an adequate evaluation of a potential donor to minimize the risks and to maximize the protection of the donor. The same paper states the absolute and relative contraindications for living kidney donation.

Even so, for living donation, we have to expose a healthy individual, the donor, to major surgery, with its known physical, economic, and social risks. First of all, there is an immediate post-surgical mortality risk, calculated in 0.03% in 1992¹⁷ and 3.1/10000 kidney donations in 2010¹⁸. According to the same source, surgical mortality is higher in men, in blacks, and in donors with hypertension. Nonetheless, the long-term risk of death is similar for live donors and age- and comorbidity-matched NHANES III participants (stratified by age, sex, and race)¹⁸. In 1997, Fehrman-Ekholm and co-workers showed that the life expectancy of kidney donors was similar, or even longer, than that of the general population¹⁹. The better survival is related to the fact that only healthy persons can become donors. In fact, donors are among the healthiest in the population. A more recent study showed that kidney donors have a normal life span, with an excellent quality of life²⁰.

The long-term medical risks for donors have been studied as well. Living donors live with the possibility that they may develop chronic kidney disease (CKD) later in life. Kasiske and colleagues, in 1995, were the first to study the consequences of reduced renal mass in humans²¹. These investigators undertook a meta-analysis and concluded that unilateral nephrectomy causes, on average, a decrease of 17 ml/min in the glomerular filtration rate (GFR). This reduction tended to improve every ten years of follow-up; a progressive increase in proteinuria was noted, mainly in those with renal agenesis or with more than 50% reduction in renal mass, and was negligible after trauma or kidney donation. Nephrectomy did not affect the prevalence of hypertension. From this study, investigators concluded that the long-term medical risk of CKD for a healthy donor after a unilateral nephrectomy is small²². Previously, Najarian, in 1992, had demonstrated no evidence of progressive renal deterioration or other severe disorders comparing donors and siblings¹⁷.

Despite these encouraging results, the absence of proof in medical risks is not proof of absence²³, and we should not underestimate the unpredictability of long-term medical complications.

Two studies reported the inclusion of donors on kidney transplant waiting lists as potential recipients^{24,25}. Donors can have an asymptomatic familial disease at donation [related to gene abnormalities – Alport, segmental and focal glomerulosclerosis (FSGS) or autoimmunity], can develop cancer (renal cell), or can develop metabolic syndrome (obesity, hypertension, glucose intolerance, diabetes), with all these well-known risk factors for kidney dysfunction. Recent findings also reported that pregnancies post-donation are at increased risk of adverse outcomes. Importantly, a 7-fold increase in the adjusted risk of preeclampsia was shown in post-donation pregnancies²⁶ and gestational hypertension was more likely to be diagnosed in living kidney donors than in matched non-donors with similar indicators of baseline health²⁷.

However, the rate of ESRD in donors is calculated to be 0.04%, comparable to the rate of ESRD in the general population (0.03%). Nevertheless, prospective registration and studies of living kidney donors are essential to protect living donors and preserve living kidney donation.

Two recent matched cohort studies^{28,29} published in 2014, revealed that over a 15-year period, kidney donors had an increased risk of ESRD and cardiovascular mortality compared with a matched cohort of healthy non-donors, though the absolute risk increase was small, below 1%^{28,29}. These findings need further confirmation.

With the current data, we can conclude that donation does not decrease lifespan and that renal failure occurs in a slight fraction of donors, but less frequently than in the general population. In Portugal, after the medical decision, the proposal for living donation is presented to the Verification of Admissibility for Transplantation Entity, and this body has to give its assent to proceed with the donation, as legislated³.

■ Principle of Autonomy

The donor has the right to informed consent and has to be in possession of all the relevant information related to the donation¹⁴, namely the surgical risks, as established by articles nº 7 and 8 of Law 22/2007³. In

Portugal, donors have the right to compensation for damage arising from the procedure, as indicated in Article nº 9 of the same law. The clarification from the medical team should not be confused with the incentive to donation in life. Further to a description of all potential damage, it is necessary to discuss the risk of recurrence of the receptor's primary disease, with consequent loss of graft function.

Is the primary renal disease an impediment to donation?

The receptor's renal disease is an important issue, since all forms of glomerulonephritis (GN) may recur after kidney transplantation. Nearly 10 to 20% of GN patients will have a recurrence of the disease in the allograft, and 50% of them will lose their graft³⁰, with this having a negative impact on long-term graft survival. Currently, recurrent disease is third-leading cause of graft loss³¹. Nonetheless, the risk of recurrence differs according to GN category.

Complement regulation disorders, particularly arising from complement alternative pathway deregulation – such as dense deposits disease, and a few cases of a familial haemolytic uraemic syndrome – have a near 100% rate of recurrence in kidney transplant. The consequence is loss of kidney function, and, therefore, in those cases is not ethically accepted to proceed with a living donation³².

However, other glomerulonephritis have a lower risk of recurrence. In the case of FSGS, nearly 30% of patients will present a recurrence in the first kidney allograft. The risk of relapse of the disease in the second graft in patients who lost their first due to recurrence may approach 100%³³. Recurrence risk is higher in living donor transplant paediatric recipients, and graft loss caused by recurrent FSGS is significantly greater in children receiving living donor transplants compared with deceased donor transplants³³⁻³⁵. Moreover, this is not exclusively linked to FSGS; it seems that for most GN, the risk of recurrence of primary disease is higher in live donor related kidney transplants than in deceased kidney donor transplants^{30,33,36}.

It is accepted that, in the case of a patient's first kidney transplant, when no one knows if the disease is going to recur, we have to allow the procedure, but we have to explain clearly the risks of recurrence. Donation could still be encouraged in carefully selected patients (and donors). Donors and recipients have to be aware of the potential hazards. Patients with

previous graft loss due to recurrent disease should be evaluated with caution.

■ Principle of Justice

The medical team must ensure the principle of justice, allowing only the donation from healthy subjects³.

Also, donate to whom?

Portuguese law allows donation between related and unrelated persons, as well as altruistic donation³.

It seems that donation between individuals who have a relationship with each other, whether or not genetically related, is ethically accepted. Donation from parents to children and between partners is morally permitted. In both cases, there is a solid and emotional relationship between donor and receptor. In the first case, the donor is older than the receptor, while in the second case, partners have identical ages.

Donation from a son to a parent is not consensual. It is a donation from a younger person to an older one, and the donor's average life expectancy is much higher than that of the organ recipient. One of the main risks for development of CKD, independent of the type of renal disease, is a positive familial history of CKD, particularly in the cases of 1st-degree relatives. Therefore, the donor may have the misfortune of developing CKD in the future, irrespective of renal function at the time of evaluation for donation. Since life expectancy is growing, the donor will live longer, with less renal mass, fewer nephrons, increasing the possibility of CKD or even for ESRD in old age. We do not know the medical consequences from nephrectomy with a life expectancy of 80 years. Nevertheless, we cannot prohibit kidney donation in these circumstances. If the same son wanted to donate the kidney to his brother, is it so different? In addition to an evaluation of the risks, we should also study the benefits of donation, and the harms from denying patients the opportunity to donate³⁸. In any case, the possible psychological coercion from the recipient will have to be scrutinized and excluded, and this is particularly relevant in the case of sons and spouses, who may feel pressured to donate their kidney, even when that is not their will.

One last question can arise from potential kidney living donors donating their organs to a non-related patient, such as a friend. Can this liberalization open a door to organ trafficking and transplant tourism and

commercialism? In 2008, a position paper from the medical community, the Declaration of Istanbul, it was published. The Declaration clarifies the issues of transplant tourism, trafficking and commercialism and provides ethical guidelines for practice in organ donation and transplantation³⁹.

■ CONCLUSION

The best therapeutic approach in ESRD patients is living kidney transplantation, which offers better survival than dialysis or cadaveric renal transplantation. From the current literature, we can see if there's evidence that donors face reduced short, mid and long-term risks. The most important is a clarification by an informed consent and a favourable risk/benefit ratio for the donor.

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