



Living Kidney Donor Evaluation: A Simplistic Approach

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Donating an organ is donating a new life. This is a remarkable act of the donor, and due to this donated organ, transplantation has become a routine practice with miraculous results, but the process of organ procurement, donation, and harvesting is not a simple one as organ transplantation sounds fascinating. This is a major undertaking and serious responsibility which rests on the shoulders of the medical community, involved in the human organ transplantation, especially from the live donors to safeguard donor health. Kidney donation principle is candid which states that one person on dialysis is better than two on dialysis. Live kidney donors are superior to the cadavers. There are exhaustive protocols for kidney donor evaluation, and guidelines vary among different countries. This article will outline the practical approach of donor evaluation by employing conventional tools of basic medical practice and help this complex process be simplified and swift and practicable. Detail history, meticulous physical examination, and thorough laboratory and radiological workup must be adopted by the transplant centers which has maximum beneficial outcome by aiding pickup donor health issues. Evaluation process can be extended further based on the abnormality detected during this workup which guides appropriate action to rectify the problem, thus protecting donor by precluding donation cost-effectively. Major point to be stressed through this article is protecting the donor health not only during the postoperative period but also providing lifelong donor follow-up.

Key words: Organ donation, kidney transplantation, donor health

INTRODUCTION

This is a proven fact that kidney transplantation is the best renal replacement modality for end-stage renal disease (ESRD) population in terms of their survival, longevity, and quality of life. Living donation has been considered advantageous over cadaveric organs due to the liberty of planning, simplistic way of logistic arrangement, and favorable outcomes postoperative. Journey of kidney transplantation initiated with organs from the live donors, but nowadays more kidneys are available from cadaveric donation system as well, either from brain or cardiac dead donors. Benefit of cadaveric organs has resulted in the expansion of the organ pool, thus helping suffering humanity. Live-related donations have been declined as compared to unrelated donations over a period of time.¹ Obtaining an organ from a living donor is a major undertaking which merits detail donor evaluation in order to make sure that individual is fit enough to continue healthy living after donation with periodic health surveillance over a prolonged period of time in fact lifetime. Kidney donor evaluation is based on a very

simple principle which states that one person is better than two on dialysis which supports that process of organ retrieval is a major undertaking which needs exhaustive and extensive evaluation for the confirmation of donor health status.

There are many regulatory bodies governing the protocol for the living kidney donation process with the utmost aim laid on the principle of donor safety. Ideally, there should be a National Level Regulatory Body with a legal framework to monitor transplantation activity. This is the responsibility of this organ procurement body to formulate a national policy and procedures and issue guidelines covering all the possible aspects of the transplantation. This organization must be held responsible to regulate and supervise legally, ethically, and professionally all the steps involved in human transplantation and maintain transparency throughout, including obtaining consent, removal of the organ from the human body, its storage, transport and transplantation, and donor follow-up.

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EVALUATION STEPS

Based on the extensive literature search, this article outlines steps for assessment and suitability of a candidate for donor nephrectomy. Wealth of evidence has been gathered based on the guidelines from the British Transplant Society (BTS), Organ Procurement and Transplantation Network (OPTN) and Kidney Disease Improving Global Outcomes (KDIGO) published in 2017.³ This is a stringent evaluation process which is based on the multidisciplinary team approach involving independent and active participation of various stakeholders involved in the job. Participants include donor, social service, transplant coordinators, psychologist, psychiatrist, physician, nephrologist, and surgeon. Their participation and close coordination should be without bias, transparent, and without any agendas other than donor protection, including obligatory role of recovery center in postdonation care with follow-up surveillance.³ Evaluation process should be steered with following recommendations:

1. Donor age is a considerable fact. General consensus suggests it is desirable that donor must be 18 years or above; however, there is no upper limit for the age as depicted in one American study. Donors above 60 years usually have reduced renal functions, means estimated glomerular filtration rate (eGFR) below 60 mL/min which could be a significant risk to the donor afterward, showed in a retrospective study that compared outcome between two donor groups where age 60 years was the cutoff limit.³ Few centers in America accepting donors up to 75 years. This has been a proven fact that graft survival is better with younger donors. Donor age <18 years is considered absolute contraindication in most centers. Old age donors should be considered after careful evaluation with more detail discussion regarding risks benefits ratio.⁴ Careful donor selection is the key to success. This fact has been supported by an American study which no mortality difference as compared to healthy nondonor population.⁵ A study from the United States proposed incidence of end-stage renal disease/10,000 donors in different donor age groups, 29 for donors 18–39 years, 17 for those 40–49 years, 55 for those 50–59 years, and 70 for those over 60 years of age⁶
2. History including specific complaints and concerns holds key importance. Questionnaire-based systems review usually picks up the significant points. Past medical problems, surgeries, drugs, and allergies must be inquired along with any particular disease running in the family. Social history must be probed deeper with occupational details, hobbies, and habits including tobacco, alcohol, and recreational drugs use. Inquire exposure to animals, pets, and sun. Traveling details may be helpful to guide about specific

diseases endemic in certain areas of the world. Psychological evaluation including details related to thoughts, mood and attitude toward life, any suicidal thoughts, and depressive ideas. Clinical examination must proceed after this interview. Based on the history and physical findings, particular investigation can be added into the standard pretransplant workup

3. Next step is blood group and human leukocyte antigen (HLA) typing, cornerstone of transplantation workup.^{7,8} Although some centers are transplanting against ABO and HLA incompatibilities with favorable patient and graft survival, this does not preclude these tests to perform.^{8,9} It is the standard practice to do HLA typing, crossmatching, and grouping between donor and recipient.⁸ Rhesus antigens once thought to be unimportant, but now evidence advocates that its mismatch results rejection episodes which could result in decreased allograft survival. On the basis of this typing and crossmatching results, donors are triaged accordingly for paired exchange programs, desensitization protocols, risk stratification, and preempting treatment strategies which will dictate graft and patient survival ultimately.¹⁰ It is recommended that blood grouping and tissue typing should be performed twice before the transplant, in the beginning of workup and immediately prior to transplant
4. Laboratory evaluation includes complete blood picture, coagulation, liver and renal functions, lipids, bone profile, blood sugar with glycosylated hemoglobin, viral serology for hepatitis, HIV, cytomegalovirus (CMV), Epstein-Barr virus (EBV), and parvovirus. Viral screen should be done or repeated if done earlier closer to the donation time preferably within a month pretransplant. The aim is to minimize risk of transmitting infections to the recipient. In case of CMV or EBV donor, seropositivity recipient must be informed clearly about the potential risk of developing CMV infection or posttransplant lymphoproliferative disorder, respectively, during the posttransplant life. HIV is contraindication to donation. Syphilis is considered as a part of routine screening as mentioned in the 2013 guidelines of UNOS and SEN-ONT (2010). Tuberculosis (TB) evaluation is mandatory for those living donors who belong to TB endemic area or high risk for TB. Latent TB infection is screened with purified protein derivative or interferon-gamma release assay.¹¹ Active TB infection is also mentioned as a contraindication in the guidelines of Amsterdam Forum (2005). Strongyloides, *Trypanosoma cruzi*, Chagas, toxoplasma antibodies, and West Nile virus should also be screened if donor belong to or has traveled to endemic areas¹²⁻¹⁶
5. Particular attention is to be paid to evaluate diabetic status of the donor, as it is one of the most common diseases to

affect donor single kidney and cardiovascular (CV)-related events. For all high-risk candidates, BTS and the European best practices recommend to perform oral glucose tolerance test due to policy of consideration of diabetics as a donor but in exceptional circumstances. These include cases with impair fasting sugars, family history of diabetes, and history of gestational diabetes. Diabetes Types 1 and 2 is associated with diabetic complications, uncontrolled hypertension, and obesity is a contraindication for donation. To consider individuals with Type 2 diabetes for donations a stringent risk stratification of donor is required for possibility of developing future kidney or heart diseases with a single remaining kidney.¹⁷ Based on the systematic review, KDIGO allows old age donors with Type 2 diabetes who fall into low-risk category, but according to the OPTN, diabetes comes under exclusion criteria. Most centers defer diabetic donors.^{18,19} A Japanese study reported equal survival benefit in the donors with and without glucose intolerance over a longitudinal follow-up of 7.6 years²⁰

6. Urine analysis is performed to detect protein, hematuria, and infections. Further tests can be performed based on the history and other investigative workup including calcium oxalate, uric acid, and cystine estimation. It is suggested to begin with urine dip stick, microscopy, culture, protein creatinine ratio on a random urine sample, and 24-h urinary protein estimation. Albuminuria is a sensitive indicator of kidney injury.²¹ Detection of albumin-to-creatinine ratio on a urine sample suggests reconfirmation by albumin excretion rate and 24-h protein loss quantification.⁴ Acceptable albumin excretion rate is <30 mg/day, more than 100 mg/day is contraindication to donation and individuals having albuminuria in between 30 and 100 mg/day is considered case-to-case basis⁴
7. Hematuria is defined as the presence of >3 red cells/high power field in a urine sample.²² It should be checked twice during the evaluation period. Persistent hematuria needs further evaluation with renal tract imaging, cystoscopy, or even kidney biopsy before consideration for donation. Cystoscopy is recommended by BTS for all above 45 years with hematuria. Donors are accepted only if workup, as mentioned turns out negative
8. Donors with a history of renal stones need evaluation with urinary stone panel²³ and imaging, especially including computed tomography (CT) scan for the bone protocol. BTS guidelines are not clear in the presence of a stone, but it is recommended that active renal stone disease and obvious metabolic abnormalities with a risk of nephrolithiasis should be dealt with a specialist advice. Without this, it precludes donation. Risk includes low citrate and high calcium and oxalates refractory to corrective measures
9. GFR estimation should be done in all. Estimation of GFR is by 24-h creatinine clearance and scintigraphy with creatinine ethylenediaminetetraacetic acid scan. Acceptable level is 90 ml/min/1.7 m² based on the systemic reviews.⁴ No donor should be accepted if there is a potential risk of fall of predicted GFR below a minimum standard which is set as 37.5ml/min at the age of 80 yrs. Disparity in renal size of more than a centimeter merits further studies with DMSA scan to estimate split renal functions and anatomy. Split difference of 10% in renal functions is significant and recommendation is to use kidney with lesser function.
10. Imaging is the most important part of donor assessment. Tools include ultrasound, CT, and magnetic resonance imaging abdomen and pelvis with contrast. CT angiography is as good as conventional renal angio with digital subtraction angiography, in fact, it is cost-effective. These images provide very vital information in terms of evidence of the presence of two kidneys, to assess renal size, structure delineating anatomy of renal tract, drainage system, presence of any anomaly, and stone or a malignant growth. It also helps outlining renal vasculature and other great vessels and organs helping to decide suitability of donor and plan anastomosis and surgical techniques
11. CV system (CVS) evaluation holds a paramount importance in donor evaluation. This situation is usually encountered when parents want to donate. This is a proven fact that cardiac events are the most common causes of morbidity and mortality in chronic kidney disease patients and leading cause of death with a functioning graft. Extensive workup is required to rule out occult cardiac disease in those who have risk factors which include family history of cardiac events in the first-degree relatives below 55 years of age, smoking, and dyslipidemia. Initial coronary assessment include history, physical examination including functional capacity, electrocardiogram, and echocardiography. Functional capacity is assessed based on metabolic equivalent task score (METS). METS >4 is considered normal and score below 4 merits assessment with more specialized investigations including coronary angiogram. BTS suggest a scoring system for CVS risk stratification. Score >10 is a contraindication for donation. BTS recommends defer all donors with a history of coronary artery disease and have low threshold for CV risk assessment as mentioned above
12. Obesity has certain serious consequences on the kidneys and usually associated with comorbid. Acceptance of obese donors varies among centers.⁴ BTS has no clear guidelines for obese donors, but it recommends donors with BMI more than 35 to reduce weight prior to donation and careful evaluation for comorbid which can pose threat to a donor in the long run with a solitary kidney. A meta-analysis from the

US donor population based on the 20 years donor follow-up showed a strong associated of obesity and ESRD^{23,24}

13. Hypertension is a commonly prevalent and frequently encountered conditions such as diabetes and obesity. BTS has clear recommendations that mild-to-moderate hypertension without any end-organ damage which is controlled by 1–2 drugs is not a contraindication for donation.²⁵ Evidence of end-organ damage and requirement of more than two antihypertensive is a contraindication for donation.⁴ Particular attention to be paid to diagnose white coat and mask hypertension accurately by adopting ambulatory monitoring as well in order to avoid false values²⁶
14. Any active malignancy and history of treated cancer exclude donors.^{27,28} These include cancers of blood, lung, breast, testicles, melanoma, and choriocarcinoma.²⁹ KDIGO suggests donors with a history of low-risk-treated cancers can be accepted for donation if risk of transmission or remission is very low based on the extensive pretransplant evaluation.²⁸ OPTN, based on the revised criteria in 2016 allows donors to donate who have undergone eradication with the removal of malignant organ such as renal cell carcinoma *in situ* with no chance of recurrence after the informed consent of the recipient.^{30–33} Similarly, donor with adult polycystic kidneys can be accepted provided thoroughly screened for any possibility of malignant transformation, thus by protecting both donor and recipient.⁴ OPTN data suggest donors are at not at higher risk of developing cancers as compared to the general population, in fact, nonskin cancers were found to be lower among donors, but higher incidence of prostatic carcinoma was observed³⁴
15. Familial diseases should also be considered into account, particularly thin basement membrane disease and Alport's syndrome. These conditions should be suspected based on the family history of hematuria and renal failure with deafness. Once suspected, these should be screened extensively by clinical geneticist. Females with X-linked Alport's can be considered as donors if above 45 years of age having normal renal profile without proteinuria or deafness.³⁵ Sickle cell disease is an absolute contraindication for donation. Candidates with sickle cell trait should be considered for donation after detail workup
16. Psychosocial assessment is another important aspect to foresee long-term consequences of donation on donor health. This includes taking account of job, pastimes and hobbies, social, financial, and emotional support services. Habits of smoking, alcoholism, or any other high-risk behaviors should be explored properly, and future risk must be anticipated and explained. Donor should be motivated and supported to adopt a healthy lifestyle before donation.³⁶

Periodic assessment is necessary to observe the compliant behavior. Living with a solitary kidney and these risk factors precludes donation process which should be clearly told to donor

17. After the consideration of suitability of a donor, informed consent should be obtained from the candidate by explaining the operative procedure and associated risks involving morbidity and mortality. Consent taking is a technical process which has legal implications. This should be transparent. Transplant team usually has a key member who is an independent assessor, a trained person to evaluate donor independently. He is officially assigned as independent living donors advocate. His prime role is to ensure safety of the donor and to make sure that given consent is free and impartial.³⁷ Donor has all the rights to withdraw at any time from donation, and it is the responsibility of donor assessing team to facilitate this decision.^{38,39}

DISCUSSION

The above-mentioned evaluation is a minimum possible workup which is mandatory to perform. By this means both donor and recipients will get safety benefit, having low risk of events in the journey of recovery. Need to expand evaluation process further is based on the results of the above-mentioned workup. Donor care postdonation is a concern of paramount importance and responsibility lies on health-care providers both short term and long term, fulfilling the principles of beneficence and nonmaleficence. Longitudinal care plan can be executed by rendering the services of health-care infrastructure either by the transplant center or through primary health-care centers.⁴⁰ Postoperative management involves wound care, addressing of medical and surgical issues with special attention to psychological well-being which helps to expedite recovery process. In general, by 3 months, donor is fully functional and able to perform activities independently. KDIGO guidelines recommend annual donor follow-up for blood pressure monitoring, serum creatinine with eGFR, and albuminuria estimation should be performed at least annually.⁴ A healthy lifestyle must be promoted among donor population which includes exercise, healthy diet, and avoiding tobacco use in any form. Long-term follow-up requires annual evaluation and every 2 years later on.⁴¹ Donor health surveillance is based on a holistic approach toward evaluation of diabetes, hypertension, renal parameters, urinary protein estimation, and any other new concerns. Monitoring process has lot of controversies and debates related to financial concerns.⁷ Special attention is paid to a situation of pregnancy in donors which poses no risk but needs careful and close observation during this period.

Long-term data regarding donor risk are very limited.⁴² Most

studies have shown same survival benefit with age-matched nondonors over a period of 10–18 years.⁴³⁻⁴⁷ One Norwegian study showed no mortality difference in the first 15 years after donation but revealed all-cause mortality risk of 18% in donor population as compared to 13% with nondonors at 25-year follow-up.⁴⁵ The Swiss Living Donor Health Registry provides both short- and long-term donor follow-up of donor health.⁴⁸ In Norway, follow-up starts from weeks 3–4, at 3rd month then yearly for 5 years, and every 5th year thereafter. The US health services research administration, the scientific registry of transplant recipients is meant to monitoring medical and psychosocial outcomes, postdonation.⁴⁹

CONCLUSION

In conclusion, revolution in renal transplant is a credit of donor population. Transplant confers a new life to sufferers, and this is ethical and professional responsibility of health-care workers to protect donors from harms postdonation, as their health can be at risk due to some known or unknown conditions related to or independent of kidney donation. Comprehensive donor evaluation not only includes medical assessment but also psychosocial and economic factors as well.⁴⁶ This process should be led by a team of highly motivated professionals and monitored by legal framework. National health policy must be in accord with the international guidelines with necessary amendments tailored according to local disease prevalence, special circumstances, and experiences. Health-care cost must also be considered. Donor safety and autonomy is of paramount concern. An independent member of transplant team should be responsible for maintaining transparency of the whole process and educate him in terms of healthy lifestyle and follow-up need. Donors deferred on medical grounds should get treatment immediately for the diagnosed condition, and successful donors need continuous follow-up with psychosocial support.⁴⁷ Safety to both the donor and recipient should be well-taken care of, and donor must be informed about all the steps including surgery and its possible risks, recovery period, and longitudinal follow-up with reassurance and optimism.

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Conflicts of interest

There are no conflicts of interest.

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