
بنام خداوند جان آفرین حکیم سخن در زبان آفرین

Donor Specifications in Pediatric KTx

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Informing the Potential Donor

- **The living donor must be offered the best possible environment for making a voluntary and informed choice about donation.**
- **Independent assessment of the donor and recipient is required by primary legislation.**
- **Support for the prospective donor, recipient, and family is an integral part of the donation/transplantation process.**

Efforts to prioritize children for KTX

- **Prior to 2005:**
  - Mostly from related living donors
- **In 2005:**
  - The allocation of deceased donor from **high quality** of deceased donors younger than 35 years
- **New Kidney Allocation System (KAS): 2014**
  - Pediatric patients have prioritized access to high quality kidneys from **KDPI less than 35%.**
  - Adults with high calculated panel more than 99% or with multi- organ transplantation take priority over children.

Factors determining KDPI and EPTS

KDPI (kidney donor profile index)	**EPTS** (expected post transplant survival)
Age	Age
Height and Weight	Current Diabetes Status
Ethnicity and Race	Number of Previous transplant
History of HTN	Receiving Chronic Dialysis
History of Diabetes	
Cause of death	
Serum Creatinine	
HCV status	
Donor meets DCD criteria	

Prognostic factors influencing graft survival

1. Donor Source
2. Recipient Age
3. Donor Age
4. Ethnicity
5. HLA Matching in Children
6. Pre-sensitization
7. Immunologic factors
8. Technical Factors & DGF
9. Antibody Induction

Donor Source

1. Short and long term graft survival in all pediatric age group better in **living donor KTX**
2. 10%-20% better graft survival after 5 years of KTx
    1. Shorter cold ischemic time
    2. Better HLA matches
    3. Lower acute rejection rate
    4. Better preoperative preparation

Recipient and Donor Age

- **Recipient:**
- Younger than 2 years old: better or worse?
- Recipients younger than 11 years have better survival form deceased kidneys than other ages
- Adolescents have the poorest 5 year result than any ages: **High-risk age window**, (except for ages more than 65 years)
  - Higher rates of medication non compliance
  - Loss of medical insurance
  - Higher recurrence rate of FSGS
- **Donor:**
  - **18-49 years → 2-17 years → less than 2 years → more than 50 years**

HLA Matching

- HLA haplotype-identical sibling donors: **the best survival**
- Donor and recipient share **non-inherited maternal antigen (NIMA)** as distinct from paternal antigen (NIPA): **improve outcome**
- Sharing **HLA DR and DQ**: may decrease the risk of Ab mediated humoral rejection
- Transplants with two HLA-DR mismatches be avoided to reduce the risk of PTLD.

Immunologic factors

- Younger children:
  - Higher number of T-cell and B-cell
  - Higher CD4+/CD8+ ratio (T-helper to T-cytotoxic)
  - Increased blastogenic responses
    - Transformation of small lymphocytes into larger cells that are capable of undergoing mitosis

Assessment of Renal Function

GFR should be measured using a reference GFR procedure,

A prospective donor should not be considered for donation if the corrected GFR is predicted to fall

below a satisfactory level of kidney function within the lifetime of the donor.

A predicted GFR of at least 37.5 mL/min/1.73 m2 at the age of 80 is recommended as a minimum standard.

A living kidney donor with normal renal function before donation is at no greater risk than an individual in the general population of developing end-stage renal disease after unilateral nephrectomy.

Measurement of estimated GFR in living donors has not been validated to predict the risk of long-term kidney disease and should not be used in this context (B1).

Acceptable GFR by donor age before donation

Donor age (yr)	*Acceptable corrected GFR before donation (mL/min/1.73m2)*
Up to 46	**80**
50	**77**
60	**68**
70	**59**
80	**50**

ABO Blood Grouping and Cross-match Testing

- **Where an ABO blood group-compatible donor-recipient pair is available, this is the preferred option (A1).**
- **Where low antibody titer ABO incompatibility is present, transplantation is not precluded but should be performed in a unit with the relevant experience and appropriate support (A1).**

Donor Age

- **Old age alone is not an absolute contraindication to donation, but the medical work-up of older donors must be particularly rigorous to ensure they are suitable (A1).**
- **Both donor and recipient should be made aware that the older donor may be at greater risk of perioperative complications and that the function and possibly the long-term survival of the graft may be compromised. This is particularly evident with donors older than 60 years (B1).**

Donor Obesity

- Otherwise healthy overweight patients (body mass index [BMI] 25–30 kg/m^2) may safely proceed to kidney donation (B1).
- Moderately obese patients (BMI 30–35 kg/m^2) should undergo careful preoperative evaluation to exclude cardiovascular, respiratory, and kidney disease (C1).
- Moderately obese patients (BMI 30–35 kg/m^2) should be counseled carefully about the increased risk of perioperative complications,
- Moderately obese patients (BMI 30–35 kg/m^2) should be counseled carefully about the long-term risk of kidney disease.
- Data on the safety of kidney donation in the very obese (BMI > 35 kg/m^2) are limited and such patients should be discouraged from donating (C1).

Donor Hypertension

- Potential donors with blood pressure less than 140/90 mm Hg should be considered as normotensive and therefore suitable for nephrectomy on the basis of blood pressure (B1).
- Potential donors with “high normal” blood pressure (> 130/85 mm Hg) should be warned about the greater future risk of developing hypertension and associated cardiovascular events and the need for monitoring (which should be recommended irrespective of nephrectomy).
- Evidence of hypertensive end-organ damage, poorly controlled hypertension, or hypertension that requires more than two drugs to

Donor Diabetese

- Potential donors must have a fasting plasma glucose level checked. A level between 5.6 and 6.9 mmol/L is indicative of an impaired fasting glucose state and an oral glucose tolerance test (OGTT) must be undertaken (B1).
- Prospective donors with an increased risk of type 2 diabetes because of family history, ethnicity, or obesity should also undergo an OGTT (B1).

Proteinuria

- **The significance of microalbuminuria (ACR 3.5–30 mg/mmol) and of 24-hr urine protein of 150 to 300mg(PCR 15–30) has not been fully evaluated in living kidney donors.**
- **However, because both the risk of chronic kidney disease and cardiovascular morbidity increase progressively with increasing albuminuria, such donors require careful evaluation and counseling about the risks of donation (C2).**

Microscopic hematuria

- **If no cause is found and the donor still wishes to donate, then a kidney biopsy should be considered and is recommended if hematuria is more than 1+ on dipstick testing (B2).**
- **Glomerular pathology precludes donation, with the possible exception of thin basement membrane disease (B1).**

Donor Malignancy

- Active malignant disease is a contraindication to living donation.
- Bilateral angiomyolipomata preclude living kidney donation. Kidneys containing angiomyolipomata of 4 cm or larger should only be transplanted if ex vivo excision of the tumor is straightforward.
- Donors with low-grade skin tumors, carcinomas in situ of the uterine cervix, and primary CNS tumors can be considered as potential donors for recipients dying on wait list longing for organ transplantation

Histocompatibility Testing

British Society for Histocompatibility & Immunogenetics

Recommendations

- Patient serum samples must be sent to the histocompatibility laboratory no less than three monthly for routine antibody monitoring and also following transfusion of any blood products.
- Serum samples must be stored for potential use in future antibody screening and cross-match tests.
- Laboratory cross-match tests should distinguish T- cell and B- cell populations and between IgG and IgM antibodies.

Recommendations

- Serum samples used for cross-matching must include a current sample and, where HLA specific antibodies have been detected, samples that are representative of the patient's antibody profile, over time.
- The timing, duration, priming source, antibody titer and donor specificity should be considered when interpreting the cross-match result.

Recommendations

- The reporting of results to clinical teams should include appropriate advice on the clinical relevance of the result. The timing, duration, priming source, antibody titre and donor specificity should be considered when interpreting the cross-match result.
- Laboratories providing services for renal transplant programs must have the capability of precisely defining HLA-A, -B, -C, DR, -DQ and DP antibody specificities in their patients so that donors who should be cross-match negative can be identified.

Recommendations

- **A pre-transplant cross-match should be performed for all patients unless a programme exists for identifying those individuals who can confidently be defined as un-sensitized. Patients with no detectable HLA specific antibodies can be transplanted on the basis of a negative virtual cross-match (vXM) without waiting for a cross-match test to be performed**

Recommendations

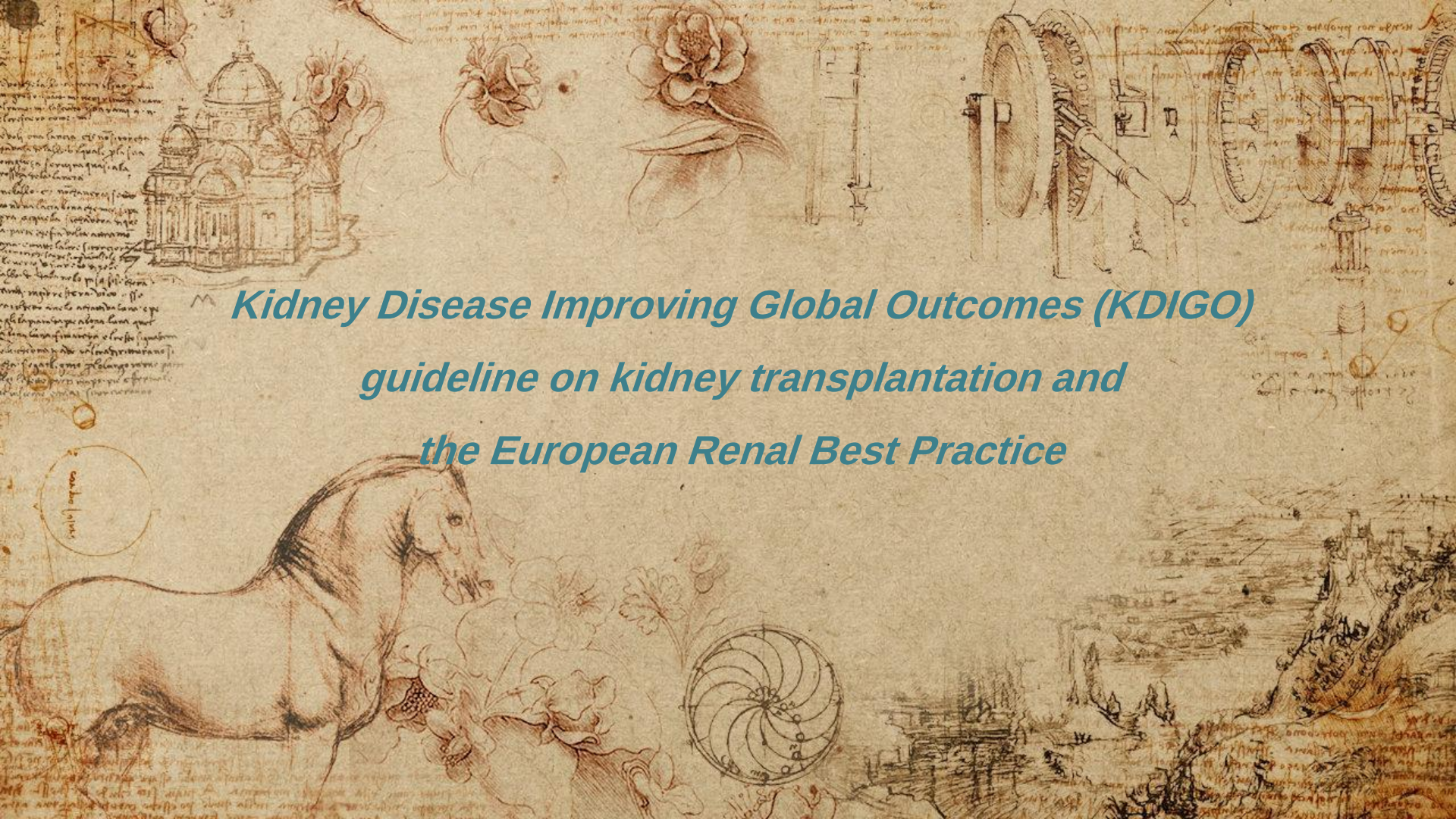
- **A patient's HLA alloantibody profile must be assessed to delineate the antigens regarded as unacceptable for transplant.**
- **Post-transplant antibody monitoring should be performed at agreed regular intervals, at the time of biopsy and in cases of suspected rejection.**
- **Samples should also be tested at times of declining graft**

Best Cross -Match Technic

- We recommend performing a complement-dependent cytotoxic (CDC) cross-match in HLA-sensitized patients to prevent hyper-acute rejection. (1B)
- We suggest that in HLA antibody negative patients with negative regular quarterly screening samples a cross-match can be omitted, unless a potential HLA-sensitizing event has occurred since last screening. (2B)

Best Cross -Match Technic

- **We do not recommend performing a Luminex or endothelial cell cross-match because their additional value needs further evaluation. (1D)**
- **We recommend a positive CDC cross-match should only be accepted as truly positive when donor-specific antibodies are known to be present. (1B)**



Kidney Disease Improving Global Outcomes (KDIGO) guideline on kidney transplantation and the European Renal Best Practice

Recipients with specific Diseases

aHUS, FSGS, CAKUT

Atypical HUS

- **We recommend that typical, proven shiga-toxin Escherichia coli-associated HUS is not a contraindication to transplantation from either deceased or living donors. (1B)**
- **We suggest considering kidney transplantation as an acceptable option (i) in kidney transplant candidates with atypical HUS (aHUS) and a proven membrane cofactor protein (MCP) mutation and (ii) in those displaying anti-complement factor H (CFH) auto-antibodies. (Ungraded Statement)**

Atypical HUS

- **Kidney transplantation in patients with aHUS should only be undertaken in centres with experience in managing this condition**
- **We do not recommend living donation from a genetically related donor in patients who are suspected to have aHUS as their underlying kidney disease unless the responsible mutation has been conclusively excluded in the donor. (1D)**

Atypical HUS

- **We recommend evaluating the potential of living donation from a genetically unrelated donor to a recipient with aHUS on a case-by-case basis. It should only be considered after appropriate counselling of recipient and donor on the risk of disease recurrence in the transplanted graft. (Ungraded Statement)**

FSGS

- We recommend that primary FSGS per se is not a contraindication to kidney transplantation from either a living or a deceased donor. (1D)
- We recommend informing the recipient and in living donation, the potential donor, about the risk of recurrence of FSGS in the graft. (Ungrade Statement)
- We recommend that when a first graft has been lost from recurrent FSGS a second graft from either a deceased or a living donor should only be transplanted after an individual risk–benefit assessment and careful counselling of the recipient and potential donor in the case of living donation. (Ungraded Statement)

FSGS

- We suggest using an updated management protocol in cases of recurrent focal segmental glomerulosclerosis. (Ungraded Statement)
- We suggest that children with steroid-resistant nephrotic syndrome undergo appropriate genotyping before wait listing them for kidney transplantation. (Ungraded Statement)

Trends in KTX Rates in Patients with CAKUT

- **Patients with both lower and upper tract congenital anomalies experienced delayed time to the first renal transplant.**
- **Patients had similar age matched graft and patient survival whether the primary source of renal demise was the congenital lower or upper tract.**

Dual-kidney transplantation

- **We recommend that before the kidneys of a cadaveric donor are discarded because they are deemed unsuitable for single transplantation, transplantation of both kidneys into one recipient (dual-kidney transplantation) is considered as an option. (1C).**
- **We suggest that in cadaveric donors where there is uncertainty about the quality of the kidneys, the decision to either discard the kidneys, or use them as a dual or a single transplant, is based on combination of the clinical evaluation and history of the recipient and donor, and when available, a standardized assessment of a pre-transplant donor biopsy. (2D)**

Dual-kidney transplantation

- **We recommend that before a kidney from a paediatric donor is discarded because due to low donor age it is deemed unsuitable for single transplantation in an adult recipient, en bloc (dual) transplantation is considered. (1B)**
- **We suggest that the option of using kidneys for en bloc transplantation is always considered for donors weighting <10 kg. (1D)**

Donor-Recipient Size Mismatch in Paediatric Renal Transplantation

Cardiovascular Complications of Size Mismatch

- If one kidney was hypothetically transplanted into a small child with a body mass of 10 kg and estimated total blood volume of 1 litre, in order to maintain that same level of perfusion it had in the adult donor, half the child's cardiac output would have to be directed to that transplanted kidney, a scenario which is clearly not sustainable.

Donor-Recipient Size Mismatch in Paediatric Renal Transplantation

- ***Graft Growth and Senescence.***
  - **An already mature adult graft will initially adapt to the paediatric recipient following transplantation; however, thereafter, it does not increase its filtration function to correlate with the increasing size and filtration demand of the growing child.**
  - **Conversely, the absolute GFR of a kidney from a paediatric donor will increase to match the child recipient's body growth, leading to a stable GFR in the recipient for many years after transplantation**

Donor-Recipient Size Mismatch in Paediatric Renal Transplantation

- ***Choice of Surgical Incision***
- ***An infant or small child has a comparatively small abdomen and thus operative field, and for a transplant to be safely undertaken with reasonable access, a midline laparotomy incision may be necessary,***

Indications of nephrectomy

- **We recommend native nephrectomy before transplantation (unilateral or bilateral) in patients with autosomal polycystic kidney disease (ARPKD, ADPKD) when there are severe, recurrent symptomatic complications (bleeding, infection, stones). (1C)**
- **We suggest unilateral nephrectomy of asymptomatic ADPKD kidneys when space for the transplant kidney is insufficient. (2C)**
- **We do not recommend routine native nephrectomy, unless in cases of recurrent upper urinary tract infections or when the underlying kidney disease predisposes to enhanced cancer risk in the urogenital tract. (Ungraded Statement)**


Thank You So Much