

ERBP Guideline on  
kidney donor and  
recipient evaluation and  
perioperative care

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## Abbreviations and Acronyms

CDC	Complement-dependent cytotoxic
ECG	Electrocardiogram
ERBP	European Renal Best Practice
FSGS	Focal Segmental Glomerulosclerosis
HUS	Haemolytic Uremic Syndrome
HVZ	Herpes Varicella Zoster
HIV	Human Immunodeficiency Virus
MICA	Major Histocompatibility Complex class I related chain-A

## Introduction

Caring for kidney transplant recipients (KTRs) requires specialized knowledge in areas as varied as nephrology, immunology, pharmacology, endocrinology, infectious disease, and cardiology. In this context of increasing complexity coupled with an exponential growth in medical literature, clinical practice guidelines (CPGs) aim at helping clinicians and other caregivers to deliver evidence-based medicine and thereby, to improve patient outcomes. Furthermore, guidelines also help to expose gaps in our knowledge, and thereby suggest areas where additional research is needed.

This guideline was developed following a rigorous methodological approach: 1) identification and selection of a representative work group, consisting of experts in transplantation (nephrologists, surgeons, immunologists) and guideline methodologists; 2) identification of clinical questions; 3) prioritisation of questions; 4) systematic literature review and critical appraisal of available evidence; 5) formulation of recommendations and grading according to GRADE; 6) comparison to existing guidelines, when available; 7) suggestions for future research.

The GRADE system allows provision of guidance even if the evidence base is weak, but makes the quality of the available evidence transparent and explicit. The strength of each recommendation is rated 1 or 2, with 1 being a 'We recommend' statement implying that most patients should receive the course of action, and 2 being a 'We suggest' statement implying that different choices will be appropriate for different patients with the suggested course of action being a reasonable choice. In addition, each statement is assigned an overall grade for the quality of evidence, A (high), B (moderate), C (low), or D (very low). Although there are reasons other than quality of evidence to make a grade 1 or 2 recommendation, in general, there is a correlation between the quality of overall evidence and the strength of the recommendation. Even if the evidence is weak, clinicians still need to make clinical decisions in their daily practice, and they often ask 'what do the experts do in this setting'? Therefore, the ERBP board opted to give guidance, even if evidence was weak or non-existing, which unfortunately is often the case in nephrology.

The draft guidelines were submitted for review to selected European experts, all ERA-EDTA members and reviewers selected by the European Society of Organ Transplantation and The Transplantation Society. Where appropriate, changes based on these comments were made in the final document. We felt this is an important step in the development of guidelines, as it fuelled the base of expertise that enhanced the overall quality of the guideline. We owe a special debt of gratitude to all those who took time out of their busy schedules to share their comments with us. They have been instrumental in improving the final guidelines.

We hope that this document will help caregivers to improve the quality of care they deliver to patients.

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## Recommendations

### Chapter 1. Evaluation of the Kidney Transplant Candidate

#### **1.1. Should we actively screen for presence of malignancy in kidney transplant candidates? Is presence or history of malignancy a contra-indication to kidney transplantation?**

We recommend screening kidney transplant candidates for cancer according to the recommendations that apply to the general population. (Ungraded Statement)

We suggest screening kidney transplant candidates for presence of kidney cancer by ultrasound. (Ungraded Statement)

We suggest screening for the presence of urothelial cancer by urinary cytology and cystoscopy in kidney transplant candidates with an underlying kidney disease associated with an increased risk of this type of cancer. (Ungraded Statement)

We recommend screening HCV and HBV-infected kidney transplant candidates for presence of hepatocellular carcinoma according to the EASL-EORTC Clinical Practice Guideline on the management of hepatocellular carcinoma. (Ungraded Statement)

We suggest that patients with current or previous cancer should be discussed with an oncologist and considered on a case by case basis. The following factors should be considered when determining the appropriate time that wait-listing should be delayed: a) the potential for progression or recurrence of the cancer according to its type, staging and grade; b) the age of the patient; c) the existence of co-morbidities, in order to define the appropriate period of time that wait-listing should be delayed. (Ungraded Statement)

#### **1.2. Under which conditions can HIV infected patients be enrolled for the waiting list?**

We recommend that HIV per se is not a contra-indication for kidney transplantation. (1C)

We recommend wait-listing HIV patients only if

- 1) they are compliant with treatment, particularly HAART therapy
- 2) their CD4+ T cell counts are  $> 200/\mu\text{L}$  and have been stable during the previous 3 months
- 3) HIV RNA was undetectable during the previous 3 months
- 4) no opportunistic infections occurred during the previous 6 months
- 5) they show no signs compatible with progressive multifocal leukoencephalopathy, chronic intestinal cryptosporidiosis, or lymphoma. (1C)

We suggest that the most appropriate anti-retroviral therapy should be discussed before transplantation with the infectious diseases team in order to anticipate potential drug interactions after transplantation. (Ungraded Statement)



### **1.3. Is there a role for immunisation against herpes varicella-zoster (HVZ) prior to renal transplantation?**

We recommend immunisation against varicella zoster virus (VZV) all paediatric and adult patients negative for anti VZ antibodies, preferable still when they are waitlisted. (1D)

### **1.4. Should haemolytic uremic syndrome (HUS) as underlying cause of end-stage renal disease preclude waitlisting for transplantation and does it influence graft and patient survival post-transplantation?**

We recommend that typical, proven shiga-toxin E-coli associated Haemolytic Uremic Syndrome (HUS) is not contra-indication to transplantation from either deceased or living donors. (1B)

We suggest considering renal transplantation as an acceptable option 1) in renal transplant candidates with aHUS and a proven MCP mutation, and 2) in those displaying anti-CFH auto-antibodies. (Ungraded Statement)

We suggest that kidney transplantation in patients with aHUS should only be undertaken in centres with experience in managing this condition and where appropriate therapeutic interventions are available. (Ungraded Statement)

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)

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)

### **1.5. Should focal segmental glomerulosclerosis (FSGS) as underlying cause of end-stage renal disease preclude waitlisting for transplantation and does it influence graft and patient survival post-transplantation?**

We recommend that primary focal segmental glomerulosclerosis 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 focal segmental glomerulosclerosis in the graft. (Ungraded Statement)

We recommend that when a first graft has been lost from recurrent focal segmental glomerulosclerosis, 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)

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)

## **1.6. Does pre-transplant alcohol and drug abuse in patients influence patient or graft survival?**

We recommend that women who drink > 40g and men who drink >60g of alcohol per day stop or reduce their alcohol consumption to below these levels. (1D)

These patients can be waitlisted, but a careful surveillance of reduction of alcohol consumption should be exerted. (Ungraded Statement)

We recommend that patients with alcohol 'dependence' should not be waitlisted. (Ungraded Statement)

Strategies to stop alcohol consumption should be offered, according to the WHO Clinical Practice Guideline. (Ungraded Statement)

We recommend that patients with an on-going addiction to 'hard drugs' resulting in non-adherence should not be waitlisted for transplantation. (1D)

## **1.7. Does pre-transplant tobacco smoking in patients influence patient or graft survival?**

We recommend that patients stop smoking before transplantation. (1B)

Smoking cessation programs should be offered. (Ungraded Statement)

## **1.8. Should obesity preclude waitlisting for kidney transplantation and is there a difference in outcomes post-transplantation between those with and without obesity?**

We recommend that patients with a BMI > 30 kg/m<sup>2</sup> reduce weight before transplantation. (Ungraded Statement)

## **1.9. Should kidney transplantation be delayed in patients presenting with uncontrolled secondary hyperparathyroidism? Does uncontrolled secondary hyperparathyroidism in the immediate pre-transplant period have an impact on transplant outcomes?**

We recommend not to refuse a cadaveric graft only because of uncontrolled hyperparathyroidism. (1D)

However, for patients on the waiting list, effort should be made to comply

with existing CKD-MBD guidelines, including parathyroidectomy, when indicated. (Ungraded Statement)

### **1.10. How should screening for potential cardiovascular disease in the potential recipient be done in a cost-effective way?**

We recommend that basic clinical data, physical examination, resting ECG and chest-X ray are a sufficient standard work-up in asymptomatic low risk kidney transplant candidates. (1C)

We recommend performing a standard exercise tolerance test and cardiac ultrasound in asymptomatic high risk patients (older age, diabetes, history of cardiovascular disease). In patients with a true negative test, further cardiac screening is not indicated. (1C)

We recommend performing further cardiac investigation for occult coronary artery disease with non-invasive stress imaging (Myocardial perfusion or Dobutamine Stress Echocardiography) in kidney transplant candidates with high risk and a positive or inconclusive exercise tolerance test. (1C)

We recommend performing coronary angiography in renal transplant candidates with a positive test for cardiac ischemia. Further management should be according to the current cardiovascular guidelines. (1D)

### **1.11. When and for which indications should native nephrectomy be performed in kidney transplant candidates awaiting kidney transplantation.**

We recommend native nephrectomy before transplantation (unilateral or bilateral) in patients with autosomal polycystic kidney disease (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)

## Chapter 2. Immunologic Workup of Kidney Donors and Recipients

### 2.1. How should HLA typing be performed in renal transplant candidates and donors?

We suggest that at least one typing is performed by molecular HLA typing of patients and donors to avoid mistakes in the classification of the HLA antigens. (2D)

We suggest that HLA typing is performed in duplicate, preferentially on separate samples obtained at different occasions to avoid logistical errors. (Ungraded Statement)

In case of sensitized patients, we recommend additional serological typing of the donor cells to be used for cross-matches in order to check the proper expression of the HLA antigens on the target cells. (1D)

For highly sensitized patients with allele specific antibodies we suggest to consider high resolution molecular typing in both recipients and donors. (2D)

### 2.2. In a renal transplant recipient, how should HLA matching be used to optimize outcome?

We suggest to match for HLA-A, -B and -DR whenever possible. (2C)

We recommend to balance the effects of HLA matching with other parameters that affect patient and graft outcomes when deciding the acceptance of a potential graft. (1D)

We recommend to give preference to an HLA identical donor and recipient combination. (1B)

We suggest to give more weight to HLA-DR matching than to HLA-A and -B matching. (2C)

We recommend to give more weight to HLA matching in younger patients, in order to avoid broad HLA sensitization that might impair re-transplantation. (Ungraded Statement)

### 2.3. In renal transplant candidates, what HLA antigens and non-HLA antigens should be defined in addition to HLA-A, -B and -DR?

We recommend to perform HLA-DQ, HLA-DP and HLA-C typing of the donor only when the intended recipient has HLA antibodies against those antigens. (1D)

We do not recommend routine typing for Major Histocompatibility Complex class I related chain-A (MICA) and other non-HLA antigens in either recipient or donor. (1D)

## **2.4. In HLA sensitized kidney transplant candidates what measures should be attempted to improve the probability of a successful transplantation?**

We recommend establishing programs to select a donor towards whom the recipient does not produce antibodies. (1C)

In recipients from cadaveric kidney donors, this aim can be achieved by an acceptable mismatch program. (1C)

In living donation this goal can be achieved by paired exchange. (Ungraded Statement)

We recommend to transplant patients with donor specific antibodies only if these abovementioned measures cannot be accomplished and after successful intervention. (1D)

## **2.5. Should in renal transplant candidates a failed allograft that still is in place be removed or left in place?**

Evidence comparing patients with a failed transplant with versus without nephrectomy is insufficient and conflictive, hampering a meaningful general recommendation on whether or not nephrectomy of failed grafts should be recommended. (Ungraded Statement)

We suggest that in following conditions an explantation of the failed kidney graft be considered: clinical rejection, chronic systemic inflammation without other obvious cause, or recurrent (systemic) infections. (Ungraded Statement)

We suggest to continue low level immunosuppression and to avoid a nephrectomy of a failed graft when residual graft urinary output is >500ml/day and there are no signs of inflammation. (Ungraded Statement)

## **2.6. In renal transplant candidates, what technique of cross-match should be used to optimize outcomes?**

We recommend a complement-dependent cytotoxic (CDC) cross-match be performed in HLA sensitized patients to prevent hyperacute 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)

We do not recommend to perform Luminex cross match, 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)

## **2.7. In renal transplant candidates planned to undergo living donor transplantation but for whom the available donor is ABO incompatible, what measures can be taken to improve outcome after transplantation?**

We recommend both inhibition of antibody production and ABO antibody removal before transplantation applied together in one and the same validated protocols. (1C)

We recommend transplantation of an ABO incompatible kidney only if the ABO antibody titre after intervention is lower than 1:8. (1C)

We suggest to consider paired exchange when available. (Ungraded Statement)

## **2.8. In previously transplanted patients, what is the effect of repeated mismatches for HLA antigens on outcome, as compared to avoiding repeated HLA mismatches?**

We recommend that repeated HLA mismatches are not considered a contra-indication for transplantation in the absence of antibodies against those repeated mismatches. (Ungraded Statement)

We suggest that the presence of antibodies against the repeated mismatch detectable by other techniques than CDC be considered as a risk factor rather than a contra-indication. (Ungraded Statement)

## **Chapter 3. Evaluation, Selection and Preparation of Deceased and Living Kidney Donors.**

### **3.1. When is dual kidney transplantation preferred over a single kidney transplantation?**

We recommend that before the kidneys of a cadaveric donor is 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 on 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 standardised assessment of a pre-transplant donor biopsy. (2D)

We recommend that before a kidney from a paediatric donor is discarded because it is deemed unsuitable for single transplantation in an adult recipient, en bloc transplantation is considered. due to low donor age for single transplantation in adult recipients, en bloc transplantation is considered. (1B)

We suggest that the option of using kidneys for en bloc transplantation is always considered for donors weighting less than 10 kg. (1D)

### **3.2.**

#### **Which perfusion solution is best suited for kidney preservation in recipients of living donation?**

#### **Which perfusion solution is best suited for kidney preservation in recipients of deceased kidney donation?**

There is insufficient evidence to favour a particular preservation solution for kidneys that carry a low risk of delayed graft function. (Ungraded Statement)

We recommend not using Eurocollins as a preservation solution for kidneys that carry a high risk of delayed graft function (long projected CIT, extended criteria donors). (1B)

### **3.3. Is machine perfusion superior to standard perfusion?**

There is conflicting data regarding the generalizability of the benefit of machine perfusion over static cold storage. Until further evidence emerges, no firm recommendation for the use of machine perfusion in preference to cold storage can be made. (Ungraded Statement)

### **3.4. Is there a critical cold ischemic time beyond which a donated organ should be discarded?**

We suggest that cold ischaemia time is kept as short as possible. (2D)

We recommend keeping cold ischaemia time below 24 hours when transplanting kidneys from donors after brain death. (1B)

We recommend keeping cold ischaemia time less than 12 hours when using kidneys from donors after cardiac death. (1D)

We recommend that the decision to use donor kidneys with a cold ischaemia time of more than 36 hours should be made on a case per case basis. (1D)

### **3.5. On which criteria should we select living kidney donors to optimize the risk/benefit ratio of their donation?**

#### **General remarks**

We recommend encouraging living kidney donors to exercise on a regular basis and when relevant, to lose weight and stop smoking. (1C)

We recommend that the individual risk of donation should be carefully discussed with the donor, taking into account the situation of both donor and recipient. Ideally, this should be done using standardised check lists to ensure all items are discussed. (Ungraded Statement)

We suggest that the donor be evaluated by an independent physician who is not part of the transplant team and is not involved in the daily care of the recipient, and when possible, by a psychologist. (Ungraded Statement)

We recommend that the process of donation is stopped should any doubt on donor safety arise, especially in younger donors, or when the benefit for the recipient is limited. (Ungraded Statement)

We recommend that the simultaneous presence of more than one risk factor (hypertension, obesity, proteinuria, impaired glucose tolerance, haematuria) precludes donation. (Ungraded Statement)

#### **Hypertension**

We recommend considering potential donors with a blood pressure <140/90 mmHg on at least three occasions without antihypertensive medication, as normotensive. (1C)

We suggest measuring ambulatory blood pressure in potential donors who have office hypertension (blood pressure >140/90 mmHg) or who are taking pharmacological treatment for hypertension (2C)

We suggest well-controlled primary hypertension, as assessed by ambulatory blood pressure <130/85 mmHg, under treatment with maximum 2 anti-hypertensive drugs (diuretics included) is not considered a contra-indication to living kidney donation. (2C)



We recommend that in hypertensive donors with evidence of target organ damage such as left ventricular hypertrophy, hypertensive retinopathy, and micro-albuminuria, donation should be discouraged. (1C)

## **Obesity**

We suggest a BMI above 35 kg/m<sup>2</sup> is a contraindication to donation. (2C)

We recommend counselling obese and overweight donors for weight loss before and after donation. (Ungraded statement)

## **Impaired glucose tolerance**

We recommend diabetes mellitus is a contraindication to donation, other than in exceptional circumstances. (1D)

We suggest impaired glucose tolerance is not an absolute contraindication to donation. (2C)

## **Proteinuria**

We recommend to quantify urinary protein excretion in all potential living donors. (1C)

We recommend overt proteinuria is a contra-indication for living donation (24-hour total protein > 300 mg or spot urinary protein to creatinine (mg/g) ratio >300 (>30 mg/mmol). (1C)

We recommend that potential living donors with persistent (more than 3 measurements with 3 months interval) proteinuria <300mg/24hrs be further evaluated by quantification of micro-albuminuria to assess their risk of living donation. (Ungraded statement)

We suggest to consider persistent (more than 3 measurements with 3 months interval) micro-albuminuria (30-300mg/24hrs) a high risk for donation. (Ungraded statement)

## **Haematuria**

We recommend considering persistent haematuria of glomerular origin as a contraindication to living donation, because it may indicate renal disease in the donor. (1B)

However, we acknowledge thin basement membrane disease might be an exception. (Ungraded statement)

## **Old age**

We recommend that old age in itself is not a contraindication to donation. (1B)

### **3.6. What lower level of kidney function precludes living donation**

We recommend that all potential living kidney donors should have their glomerular filtration rate (GFR) assessed. (1C)

We recommend that in cases where more exact knowledge on GFR is needed or where is doubt regarding the accuracy of GFR from estimation methods, a direct measurement of GFR should be undertaken by exogenous clearance methods. (Ungraded Statement)

We recommend that all potential donors should have a predicted GFR that is projected to remain above a satisfactory level after donation within the lifetime of the donor as indicated in the graph below. (Ungraded Statement)

### **3.7. What are the risks of pregnancy in a woman with a single kidney after living kidney donation?**

We recommend informing women of childbearing age that as they are a selected from a very healthy subpopulation, donation increases their individual risk from below that of the general population, to that of the general population. (1B)

### **3.8. What is the best surgical approach for living donor nephrectomy for the donor? What is the best surgical approach for living donor nephrectomy for the recipient?**

For living donor nephrectomy we suggest either a minimally invasive or laparoscopic approach rather than a flank subcostal retroperitoneal one. The choice between minimal invasive and laparoscopic procedure should be based on the local expertise. (2C)

## Chapter 4. Perioperative Care of the Kidney Transplant Recipient

### 4.1. What are the indications for an additional haemodialysis session in the recipient immediately before the transplantation procedure?

We recommend to not routinely perform a haemodialysis session immediately before the actual transplantation procedure unless there are specific clinical indications. (1C)

When additional haemodialysis is performed immediately before the transplantation procedure, we recommend that ultrafiltration is not used unless there is evidence of fluid overload. (1C)

### 4.2. Does the use of central venous pressure measurement as a guidance tool for fluid management in kidney transplant recipients improve the outcome after transplantation?

We suggest that central venous pressure is measured and corrected in the early post-operative period to prevent hypovolemia and delayed graft function. (2D)

### 4.3. In kidney transplant recipients during the perioperative period, does the use of intravenous solutions other than 0.9% sodium chloride improve patient and/or graft outcome?

There is no evidence to prefer one type of solution (crystalloids versus colloids, normal saline versus Ringer) for intravenous volume management of the recipient during kidney transplant surgery. (Ungraded Statement)

In view of the available data in the general literature, and in line with the ERBP position on prevention of AKI, we suggest to be cautious with the use of starches in the perioperative kidney transplant patient, although specific data on the use of starches in the perioperative period in kidney transplant recipients are lacking. (Ungraded Statement)

We recommend to monitor for metabolic acidosis when normal saline is used as the only intravenous fluid in the perioperative and postoperative period. (1B)

### 4.4. Does the use of dopaminergic agents (dopamine and its alternatives) improve early postoperative graft function?

We do not recommend the use of 'renal doses' of dopaminergic agents in the early postoperative period, since it does not influence graft function or survival. (1B)

#### **4.5. Should we use prophylactic antithrombotic agents during the perioperative period?**

We do not recommend routinely using low molecular weight heparin, unfractionated heparin or aspirin before transplantation to prevent graft thrombosis. (1B)

#### **4.6. In renal transplant recipients, what are the effects of using a JJ stent at the time of operation on renal outcomes?**

We recommend prophylactic JJ stent placement as a routine surgical practice in adult kidney transplantation. (1B)

We suggest that when an JJ stent is in place, cotrimoxazole is given as antibiotic prophylaxis. (2D)

We suggest removing the JJ stent within 4 to 6 weeks. (Ungraded Statement)

#### **4.7. What is the optimal postoperative time for removal of the indwelling bladder catheter in kidney transplant recipients?**

We suggest removing the urinary bladder catheter as soon as possible after transplantation, balancing the risk of urinary leak against that of urinary tract infection. (2D)

We recommend monitoring adverse event rates (urinary tract infection, urinary leakage) in each centre, to inform the decision over when to remove the indwelling bladder catheter. (1D)







