

European Renal Best Practice Guideline on the Management and Evaluation of the Kidney Donor and Recipient

Julio Pascual¹, Daniel Abramowicz², Pierre Cochat³, Frans Claas⁴, Chris Dudley⁵, Paul Harden⁶, Uwe Heeman⁷, Maryvonne Hourmant⁸, Umberto Maggiore⁹, Maurizio Salvadori¹⁰, Goce Spasovski¹¹, Jean-Paul Squifflet¹², Juerg Steiger¹³, Armando Torres¹⁴, Raymond Vanholder¹⁵, Wim Van Biesen¹⁵, Ondrej Viklicky¹⁶, Martin Zeier¹⁷, Evi Nagler¹⁸

¹ Coordinator work group recipient evaluation. Nephrologist. Hospital del Mar-IMIM. Barcelona (Spain);

² Chair. Nephrologist. Erasme Hospital. Université Libre de Bruxelles (Belgium); ³ Co-Chair. Paediatric Nephrologist. Hospices Civiles de Lyon. Claude Bernard University (France); ⁴ Coordinator work group Immunology. Transplant Immunologist. Leiden University Medical Centre. The Netherlands and Director at Eurotransplant Reference Laboratory; ⁵ Nephrologist. Southmead Hospital. Bristol (UK); ⁶ Nephrologist, Churchill Hospital. Oxford University (UK); ⁷ Coordinator work group donor evaluation. Nephrologist. Technical University Munich. Klinikum rechts der Isar (Germany); ⁸ Nephrologist. Nantes University Hospital (France); ⁹ Nephrologist. Parma University Hospital (Italy); ¹⁰ Nephrologist. Azienda Ospedaliero Universitaria Careggi. University of Florence (Italy);

¹¹ Nephrologist. Skopje University Hospital (Macedonia); ¹² Consultant Abdominal and Transplantation Surgery. University Hospital of Liège (Belgium); ¹³ Nephrologist. University Hospital Basel (Switzerland); ¹⁴ Nephrologist. University Hospital de Canarias. University of La Laguna. Canary Islands (Spain); ¹⁵ Nephrologist. Ghent University Hospital (Belgium); ¹⁶ Nephrologist. Institute of Clinical and Experimental Medicine. Prague (Czech Republic); ¹⁷ Nephrologist. University Hospital Heidelberg (Germany); ¹⁸ Specialist Registrar Nephrology. Ghent University Hospital (Belgium)

¹¹ Nephrologist. Skopje University Hospital (Macedonia); ¹² Consultant Abdominal and Transplantation Surgery. University Hospital of Liège (Belgium); ¹³ Nephrologist. University Hospital Basel (Switzerland); ¹⁴ Nephrologist. University Hospital de Canarias. University of La Laguna. Canary Islands (Spain); ¹⁵ Nephrologist. Ghent University Hospital (Belgium); ¹⁶ Nephrologist. Institute of Clinical and Experimental Medicine. Prague (Czech Republic); ¹⁷ Nephrologist. University Hospital Heidelberg (Germany); ¹⁸ Specialist Registrar Nephrology. Ghent University Hospital (Belgium)

¹¹ Nephrologist. Skopje University Hospital (Macedonia); ¹² Consultant Abdominal and Transplantation Surgery. University Hospital of Liège (Belgium); ¹³ Nephrologist. University Hospital Basel (Switzerland); ¹⁴ Nephrologist. University Hospital de Canarias. University of La Laguna. Canary Islands (Spain); ¹⁵ Nephrologist. Ghent University Hospital (Belgium); ¹⁶ Nephrologist. Institute of Clinical and Experimental Medicine. Prague (Czech Republic); ¹⁷ Nephrologist. University Hospital Heidelberg (Germany); ¹⁸ Specialist Registrar Nephrology. Ghent University Hospital (Belgium)

Nefrologia 2014;34(3):293-301

doi:10.3265/Nefrologia.pre2014.Feb.12490

ABSTRACT

The purpose of this Clinical Practice Guideline is to provide guidance on evaluation of the kidney donor and transplant recipient as well as on the management of the recipient in the perioperative period. It is designed to provide information and aid decision-making. It is not intended to define a standard of care, and should neither be construed as one nor should it be interpreted as prescribing an exclusive course of management. The original version of this guideline was published in *Nephrology, Dialysis and Transplantation* and this current version is a reduced article aiming to disseminate the guideline into Spanish-speaking countries and transplant communities.

Keywords: Kidney transplantation. Kidney donor. Guideline. Recipient.

Guías Europeas sobre manejo y evaluación de receptores y donantes renales

RESUMEN

El objetivo de esta Guía de Práctica Clínica es ofrecer orientación para la evaluación tanto del donante como del receptor del trasplante de riñón y para el manejo del receptor durante el periodo perioperatorio. Ha sido diseñada para informar y asistir en la toma de decisiones. En ningún caso pretende definir una norma asistencial ni su carácter debe concebirse ni interpretarse como único o prescriptivo de un manejo exclusivo. La versión original de esta guía fue publicada en la revista Nephrology, Dialysis and Transplantation. Esta versión reducida pretende colaborar en la divulgación de esta guía en los países y comunidades trasplantadoras hispanohablantes.

Palabras clave: Trasplante de riñón. Donante de riñón. Orientación. Receptor.

PURPOSE AND SCOPE

Purpose

The purpose of this Clinical Practice Guideline is to provide guidance on evaluation of the kidney donor and transplant recipient as well as on the management of the recipient in the

Correspondence: Julio Pascual
Department of Nephrology.
Hospital del Mar. Barcelona (Spain).
julpascual@gmail.com

perioperative period. It is designed to provide information and aid decision-making. It is not intended to define a standard of care, and should neither be construed as one nor should it be interpreted as prescribing an exclusive course of management. The original version of this guideline was published in *Nephrology, Dialysis and Transplantation*¹ and this current version is a reduced article aiming to disseminate the guideline into Spanish-speaking countries and transplant communities.

Scope and target population

This guideline describes the issues related to selection and evaluation of the kidney donor and transplant recipient. It encompasses aspects of immunological risk assessment and management as well as perioperative care of the recipient. It does not address prevention and treatment of complications that occur after kidney transplantation, nor does it cover immunosuppressive treatment at any stage. For these topics we refer to the Kidney Disease Improving Global Outcomes (KDIGO) guideline on kidney transplantation² and the European Renal Best Practice (ERBP) Endorsement of this guideline.³ Although many of the issues that are important for kidney transplant candidates and their donors are also important for potential recipients of other organs, we intend this guideline for the setting of kidney transplantation only. When discussing aspects of screening for and mediation of risk factors in the kidney transplant candidate, we only assess this in function of the kidney transplant that is to follow. Although many of these are relevant to other surgical procedures and to individuals with chronic kidney disease not opting for kidney transplantation, these aspects of care will not be addressed in this document. This guideline is targeted to all kidney transplant candidates and their donors irrespective of age. Occasionally, when applicable, only children are targeted, and then this is clearly indicated.

Target population perspectives

An effort has been made to capture the perspectives of the target population by adopting two strategies. Firstly, ERBP has a permanent patient representative on its board. Although he was not included in the guideline development group or in the evidence review process, drafts of the guideline document were sent out for his review and his comments were taken into account in revising drafts of the final document. Secondly, the guideline was sent out for public review before publication. All members of the European Renal Association-European Dialysis Transplant Association (ERA-EDTA) received an online questionnaire with a pre-specified answer grid. In this grid, on a scale from 1 to 5, ERA-EDTA members could express to what extent they felt the individual statements were clear, implementable and to what extent they agreed with the

content. In addition, a free text field was provided to allow for additional comments.

Target users

This guideline was written for health care professionals dealing with kidney transplantation. This includes nurses, general practitioners, transplant nephrologists, transplant surgeons and other physicians and medical professionals who directly or indirectly care for kidney transplant candidates and their living donors. It is also directly targeted at kidney transplant candidates and their living donors, to help them balance benefits and harms of various management strategies and tailor management to their personal preferences and values.

METHODS FOR GUIDELINE DEVELOPMENT

Establishment of the guideline development group

The ERBP Board members appointed the Chair and Co-chair of the guideline development group, who then assembled the guideline development group to be responsible for the development of the guideline. The guideline development group consisted of individuals with expertise in transplant immunology, adult and paediatric nephrology, transplant surgery and medicine. The ERBP Methods Support Team is a group of young nephrologists trained in guideline development and systematic review methodology. Throughout the process they contributed methodological input and assistance with literature searches—together with methodology experts at the Cochrane Renal Group in Sydney, Australia.

Defining clinical questions

Specific clinical questions were developed within the guideline development group to reflect the key issues in the management and evaluation of the kidney donor and recipient. They were structured in four chapters and comprised a total of 34 questions.

The Methods Support Team assisted the guideline development group in framing the clinical questions into a PICO format, a well-accepted methodology which requires breakdown of the clinical question with careful specification of a patient group, the intervention diagnostic test or risk factor, the comparator and the outcomes or target disease of interest.³ For each question the guideline development group and Methods Support Team agreed upon explicit criteria for the patient group, intervention or risk factor, comparators, outcomes and study design features.

Details on assessment of the relative importance of the outcomes, searching for evidence, data extraction and critical ap-

praisal of the literature, formulating and grading recommendations (GRADE), ungraded statements, writing rationale and organization of internal and external review are depicted in the original version of this guideline.¹

After the data tables were prepared, revised and approved by the guideline development group three full-day plenary meetings were held in December 2011, February 2012 and May 2012 to formulate and grade the recommendations. We used a structured approach, based on Grading of Recommendations Assessment, Development and Evaluation Working Group (GRADE) methodology to grade the quality of the evidence and the strength of the recommendations.⁴ GRADE offers a system for separately rating the quality of the evidence and grading the strength of the recommendations in the guideline. The 'strength' of a recommendation indicates the extent to which we are confident that adherence to the recommendation will do more good than harm. The 'quality' of the evidence refers to the extent to which we are confident that the estimates of effect across studies are close to the true effects.

In this reduced version, we will provide with the recommendations written by the group. In the original version the reader may find the rationale for each recommendation or suggestion, the way we translated what we found in the literature to the recommendation and the suggestions for future research.

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 contraindication 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 the 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 the 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 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 comorbidities, in order to define the appropriate period of time that wait-listing should be delayed. (*Ungraded Statement*).

Based on consensus of personal opinion, the guideline development group supported following suggestions:

- We suggest that patients with in situ cancers of the skin and uterine cervix, and patients with incidentally discovered and successfully removed kidney cancer, can be immediately registered on the waiting list.
- We suggest that patients with localized cancer of good prognosis such as cancers of the thyroid, uterus body, uterine cervix or larynx wait 1-3 years before transplantation.
- We suggest that patients with a potentially curable cancer such as localized, or curable metastatic or disseminated cancer such as testicular malignancy or lymphoma wait at least 1-3 years before transplantation.
- We suggest strongly discouraging transplantation for at least 5 years for cancers with a generally poor prognosis such as lung, stomach, brain and oesophagus cancers, melanoma and mesothelioma.
- We suggest strongly discouraging transplantation in patients with metastatic or disseminated forms of any cancer, except for testicular cancer and lymphomas.

1.2. Under which conditions can HIV infected patients be enrolled on the waiting list?

- We recommend that HIV per se is not a contraindication for kidney transplantation. (*IC*)
- 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/ μ 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. (*IC*)
- We suggest that the most appropriate antiretroviral 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 immunization against herpes varicella-zoster prior to kidney transplantation?

- We recommend immunization against varicella-zoster virus in all paediatric and adult patients negative for an-

ti-varicella-zoster antibodies, preferably when they are still wait-listed. (*ID*)

1.4. Should haemolytic uraemic syndrome (HUS) as underlying cause of end-stage kidney disease preclude wait-listing for transplantation and does it influence graft and patient survival post-transplantation?

- 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*)
- We suggest that kidney transplantation in patients with aHUS should only be undertaken in centers 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. (*ID*)
- 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 as underlying cause of end-stage kidney disease preclude wait-listing 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. (*ID*)
- 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. (*ID*) These patients can be wait listed, but a careful surveillance of reduction of alcohol consumption should be exerted. (*Ungraded Statement*)
- We recommend not wait-listing patients with alcohol 'dependence'. (*Ungraded Statement*)
- Strategies to stop alcohol consumption should be offered, according to the World Health Organization (WHO) Clinical Practice Guideline. (*Ungraded Statement*)
- We recommend not wait-listing patients with an ongoing addiction to 'hard drugs' resulting in non-adherence. (*ID*)

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

- We recommend patients stop smoking before transplantation. (*1B*) Smoking cessation programs should be offered. (*Ungraded Statement*)

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

- We recommend that patients with a body mass index (BMI) >30kg/m² 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 refusing a cadaveric graft only because of uncontrolled hyperparathyroidism in the recipient. (*ID*) However, for patients on the waiting list, effort should be made to comply with existing chronic kidney disease-met-

abolic bone disease 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?

The guideline development group decided to reformat the problem into some easier to solve subquestions:

- (1) Is it safe in asymptomatic patients at low risk to only screen for cardiovascular risk by physical examination, ECG and chest X-ray?
- (2) What is the negative predictive value of non-invasive tests such as a cardiac exercise tolerance test in asymptomatic patients with a higher risk (diabetes, older age, history of cardiovascular disease)?
- (3) What is the negative predictive value of non-invasive tests such as myocardial perfusion tests or dobutamine stress echocardiography?

By providing the answers to these questions, we hoped to substantially simplify screening for cardiovascular risk in transplant candidates, and reduce the number of patients in need of a coronary angiography, without putting them at jeopardy. As an additional question, we wondered whether there are cardiac tests predictive for increased cardiac mortality due to non-coronary artery disease.

- We recommend that basic clinical data, physical examination, resting electrocardiogram (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 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 (dobutamine stress echocardiography or myocardial perfusion scintigraphy) in kidney transplant candidates with high risk and a positive or inconclusive exercise tolerance test. (*1C*)
- We recommend performing coronary angiography in kidney transplant candidates with a positive test for cardiac ischaemia. 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 se-

vere, 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

Immunological work-up of kidney donors and recipients

2.1. How should HLA typing be performed in kidney 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 kidney transplant recipient, how should HLA matching be used to optimize outcome?

- We suggest matching for HLA-A, HLA-B and HLA-DR whenever possible. (*2C*)
- We recommend balancing 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 giving preference to an HLA identical donor and recipient combination. (*1B*)
- We suggest giving more weight to HLA-DR matching than to HLA-A and HLA-B matching. (*2C*)
- We recommend giving 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 kidney transplant candidates, what HLA antigens and non-HLA antigens should be defined in addition to HLA-A, -B and -DR?

- We recommend performing HLA-DQ, HLA-DP and HLA-C typing of the donor only when the intended re-

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 programmes 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 programme. (1C)
- In living donation this goal can be achieved by paired exchange. (Ungraded Statement)
- We recommend transplanting patients with donor-specific antibodies only if these above-mentioned measures cannot be accomplished and after successful intervention. (2D)

2.5. Should in kidney transplant candidates a failed allograft that is still 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 explanation 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 kidney transplant candidates, what technique of cross-match should be used to optimize outcomes?

- We recommend performing a complement-dependent cytotoxic (CDC) cross-match 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 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)

2.7. In kidney 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 protocol. (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 considering 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 contraindication 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 technique be considered as a risk factor rather than a contraindication. (Ungraded Statement)

CHAPTER 3

Evaluation, selection and preparation of deceased and living kidney donors

3.1. When is dual-kidney transplantation preferred over single-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)
- 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 transplantation is considered. (1B)
- We suggest that the option of using kidneys for en bloc transplantation is always considered for donors weighting <10kg. (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 DGF. (Ungraded Statement)
- We recommend not using Eurocollins as a preservation solution for kidneys that carry a high risk of DGF (long-projected CIT extended criteria donors). (1B)

3.3. Is machine perfusion superior to standard perfusion?

- There are conflictive 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 ischaemia time beyond which a donated organ should be discarded?

- We suggest that CIT is kept as short as possible. (2D)
- We recommend keeping CIT below 24h when transplanting kidneys from donors after brain death. (1B)
- We recommend keeping CIT <12h when using kidneys from donors after cardiac death. (1D)
- We recommend that the decision to use donor kidneys with a CIT of >36h 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 standardized 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 <140/90mmHg 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 \geq 140/90mmHg) or who are taking pharmacological treatment for hypertension. (2C)
- We suggest well-controlled primary hypertension, as assessed by ambulatory blood pressure <130/85mmHg, under treatment with maximum two antihypertensive drugs (diuretics included) is not considered a contraindication to living kidney donation. (2C)
- We recommend discouraging hypertensive donors with evidence of target organ damage such as left ventricular hypertrophy, hypertensive retinopathy and microalbuminuria. (1C)
- We suggest that these potential donors could be re-evaluated for disappearance of this target organ damage after appropriate treatment. (2D)

Obesity

- We suggest a BMI >35kg/m² is a contraindication to donation. (2C)

special articles

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

Proteinuria

- We recommend quantifying urinary protein excretion in all potential living donors. (*IC*)
- We recommend overt proteinuria is a contraindication for living donation [24-h total protein >300mg or spot urinary albumin to creatinine (mg/g) ratio >300 (>30mg/mmol)]. (*IC*)
- We recommend further evaluating potential living donors with persistent (more than three measurements with 3 months interval) proteinuria <300mg/24h by the quantification of micro-albuminuria to assess their risk of living donation. (*Ungraded Statement*)
- We suggest considering persistent (more than three measurements with 3 months interval) microalbuminuria (30-300mg/24h) 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 kidney disease in the donor. (*IB*)
- 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. (*IB*)

3.6. What lower level of kidney function precludes living donation?

- We recommend that all potential living kidney donors have their GFR assessed. (*IC*)
- 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 is 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 life-time of the donor. (*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. (*IB*)

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 not routinely performing a haemodialysis session immediately before the actual transplantation procedure unless there are specific clinical indications. (*IC*)
- When additional haemodialysis is performed immediately before the transplantation procedure, we recommend not using ultrafiltration unless there is evidence of fluid overload. (*IC*)

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 (CVP) is measured and corrected in the early post-operative period to prevent hypovolaemia and DGF. (*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. In view of the available data in the literature, and in line with the ERBP position on prevention of acute kidney injury, we suggest to be cautious with the use of starches in the kidney transplant recipient during the perioperative period, although specific data in this setting are lacking. (*Ungraded Statement*).
- We recommend monitoring for metabolic acidosis when normal saline is used as the only intravenous fluid in the perioperative and post-operative period. (*IB*)

4.4. Does the use of dopaminergic agents (dopamine and its alternatives) improve early post-operative graft function?

- We do not recommend the use of 'renal doses' of dopaminergic agents in the early post-operative period, since it does not improve graft function or survival. (*IB*)

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. (*IB*)

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

- We recommend prophylactic JJ stent placement as a routine surgical practice in adult kidney transplantation. (*IB*)

- We suggest that if a JJ stent is in place, cotrimoxazole is given as antibiotic prophylaxis. (*2D*)
- We suggest removing the JJ stent within 4-6 weeks. (*Ungraded Statement*)

4.7. What is the optimal post-operative 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 center, to inform the decision over when to remove the indwelling bladder catheter. (*ID*)

Conflict of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

REFERENCES

1. European Renal Best Practice Transplantation Guideline Development Group. ERBP Guideline on the Management and Evaluation of the Kidney Donor and Recipient. *Nephrol Dial Transplant* 2013;28 Suppl 2:ii1-71.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Transplant* 2009;9 Suppl 3:s1-155.
3. Heemann U, Abramowicz D, Spasovski G, Vanholder R; European Renal Best Practice Work Group on Kidney Transplantation. Endorsement of the Kidney Disease Improving Global Outcomes (KDIGO) guidelines on kidney transplantation: a European Renal Best Practice (ERBP) position statement. *Nephrol Dial Transpl* 2011;26:2099-106.
4. Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A, et al. Going from evidence to recommendations. *BMJ* 2008;336:1049-51.