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 urethral cancer by uterine 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 the screening of 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 positive patients only if: 1) they are compliant with treatment, particularly HAART therapy 2) their CD4+ T cell counts are ≥200 µL 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 adults patients negative for anti VZ antibodies, preferable when still are waitlisted. (1D)

1.4. Should haemolytic urticarial syndrome (HUS) or an underlying cause of end-stage renal disease preclude waitlisting or transplantation and does it influence graft and patient survival post-transplantation?

We recommend 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. (1C)

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)

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

We recommend performing a standard exercise tolerance test and cardiac ultrasound in asymptomatic high risk patients (older age, diabetes, history of hypertension). (1C)

We suggest 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)

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 appropriate therapeutic interventions are available. (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 recommend 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)

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

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

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 appropriate therapeutic interventions are available. (Ungraded Statement)

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 donor. (1C)

We suggest using an updated management protocol in cases of recurrent focal segmental glomerulosclerosis. (Ungraded Statement)

We recommend that patients on the waiting list, effort should be made to comply with existing CKD-MBD guidelines, including parathyroidectomy, when indicated. (Ungraded Statement)

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We recommend that patients on the waiting list, effort should be made to comply with existing CKD-MBD guidelines, including parathyroidectomy, when indicated. (Ungraded Statement)

1.8. Should obesity preclude waitlisting for kidney transplantation and does it influence graft and patient survival post-transplantation?

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

We recommend 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)

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We recommend that patients on the waiting list, effort should be made to comply with existing CKD-MBD guidelines, including parathyroidectomy, when indicated. (Ungraded Statement)
2.1. How should HLA typing be performed in renal transplant candidates and donors? We suggest that at least one typing be performed by molecular HLA typing of patients and donors to avoid mistakes in the classification of the HLA antigens. (1D) We suggest that HLA typing is performed in duplicate, preferably 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 recommend to match for HLA-A, -B and -DR whenever possible. (1C) 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. (2B) 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, -DPA and -DPB 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 (HLA-A, B and -C) 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. (1D) In living donation this goal can be achieved by paired exchange. (1D) We recommend to transplant patients with donor specific antibodies only if these aforementioned measures cannot be accomplished and after successful intervention. (2D)

2.5. Should in renal transplant candidates a failed allotransplant 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 conflicting. A hampering a meaningful recommendation on whether or not nephrectomy of failed grafts should be recommended. (Ungraded Statement) We suggest that in recipients with a non-functional renal graft, clinical evaluation should be performed. (1D) 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. (1D)

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

2.7. In renal transplant candidates planned to undergo living donor transplantation but for whom the available donor is AB0 incompatible, what measures can be taken to improve outcome after transplantation? We recommend both substitution of antibody production and AB0 antibody removal before transplantation applied together in one and the same validated protocols. (1C) We recommend transplantation of an AB0 incompatible kidney only if the AB0 antibody titer 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 these 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)


3.1. When is dual kidney transplantation preferred over a single kidney transplantation? We recommend that before the kidney of a cadaveric donor is discarded because it is deemed unsuitable for single transplantation, transplantation of both kidneys into one recipient (dual kidney transplantation) is considered as an option. (1D) We suggest that in cadaveric donors where there is uncertainty on the quality of the kidney, the decision to either discard the kidneys, or use them as a dual kidney transplant, is based on combination of the clinical evaluation and history of the recipient and donors and, when available, a standardized assessment of a pre-transplant donor biopsy. (1D) We recommend that before a kidney from a paediatric donor is discarded because it is deemed unsuitable for single transplantation in an adult recipient, an bloc transplantation is considered, due to low donor age for single transplantation in adult recipients, en bloc transplantation is considered. (1D) We suggest that the option of using kidneys for en bloc transplantation is always considered for donors weighting less than 10 kg. (1B) We suggest that the option of using kidneys for en bloc transplantation is always considered for donors weighting less than 10 kg. (1B)

3.2. Which perfusion solution is best suited for kidney preservation in recipients of living donation? We recommend to give preference to an HLA identical donor and recipient combination. (1B) 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)

3.3. What is machine perfusion superior to standard perfusion? 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). (1D)

3.4. In renal transplant candidates, what HLA antigens and non-HLA antigens should be defined in additional to HLA-A, -B and -DR? We recommend to perform HLA-DQ, -DPA and -DPB 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 (HLA-A, B and -C) and other non-HLA antigens in either recipient or donor. (1D)

3.5. Should in renal transplant candidates a failed allotransplant 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 conflicting. A hampering a meaningful recommendation on whether or not nephrectomy of failed grafts should be recommended. (Ungraded Statement) We suggest that in recipients with a non-functional renal graft, clinical evaluation should be performed. (1D) 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. (1D)

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3.7. In renal transplant candidates planned to undergo living donor transplantation but for whom the available donor is AB0 incompatible, what measures can be taken to improve outcome after transplantation? We recommend both substitution of antibody production and AB0 antibody removal before transplantation applied together in one and the same validated protocols. (1C) We recommend transplantation of an AB0 incompatible kidney only if the AB0 antibody titer after intervention is lower than 1:8. (1C) We suggest to consider paired exchange when available. (Ungraded Statement)

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

**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 state that the donor should 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. (1C)

**Hypertension**

We recommend considering potential donors with a blood pressure >140/90 mmHg on at least three occasions without antihypertensive medication, as normal. (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 (adverse effects included) is not considered a contra-indication to living donation. (2C)

We note that in hypertensive donors with evidence of target organ damage such as left ventricular hypertrophy, hypertension-related nephropathy, and microalbuminuria, donation should be discouraged. (1C)

**Obesity**

We suggest a BMI above 35 kg/m² is a contra-indication to donation. (2C)

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

**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 ratio in mg/g >300). (1C)

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

We suggest to consider donors with proteinuria >300mg/24h or with micro-albuminuria >10-30mg/24h, taking their risk into account. (1C)

**Haematuria**

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

However, we acknowledge that basement membrane disease might be an exception. (1C)

**Impaired glucose tolerance**

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

We recommend informing women of childbearing age that as they are a selected from a very healthy subpopulation, donation increases their individual life-time of the donor as indicated in the graph below. (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)

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

We recommend a haemoglobin <110 g/litre is a contra-indication to donation. (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 they are selected from a very healthy subpopulation, donation increases their individual risk below that of the general population, to that of the general population. (1C)

**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?

We recommend using minimal invasive or laparoscopic procedures. (2C)

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

**4.** 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 recommend using minimal invasive or laparoscopic approach rather than a flank subcostal retroperitoneal one. The choice between minimal invasive or laparoscopic procedure should be based on the local expertise. (2C)