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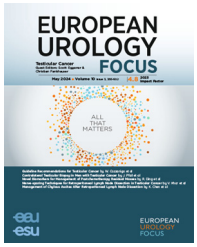

Review – Renal Disease

European Association of Urology Guidelines on Renal Transplantation: Update 2024

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Abstract

Background and objective: The European Association of Urology (EAU) Panel on Renal Transplantation released an updated version of the renal transplantation (RT) guidelines. This report aims to present the 2024 EAU guidelines on RT.

Methods: A broad and comprehensive scoping exercise covering all areas of RT guidelines published between May 31, 2020 and April 1, 2023 was performed. Databases covered by the search included Medline, Embase, and the Cochrane Libraries. Previous guidelines were updated, and levels of evidence and grades of recommendation were assigned.

Key findings and limitations: It is strongly recommended to offer pure or hand-assisted laparoscopic/retroperitoneoscopic surgery for living donor nephrectomy. One should not base decisions regarding the acceptance of a donor organ on histological findings alone, since this might lead to an unnecessary high rate of discarded grafts. For the ureterovesical anastomosis, a Lich-Gregoir–like extravesical technique protected by a ureteral stent is the preferred technique. A list of RT patients with a history of appropriately treated low-stage/grade renal cell carcinoma or prostate cancer should be made without additional delay. In the potential donor kidney, the main surgical tumoral approach is ex vivo tumor excision and finally transplantation. It is also strongly recommended to perform initial rejection prophylaxis with a combination therapy of a calcineurin inhibitor (preferably tacrolimus), mycophenolate, steroids, and an induction agent (either basiliximab or antithymocyte globulin). The long version of the guidelines is available at the EAU website (www.uroweb.org/guidelines).

Conclusions and clinical implications: These abridged EAU guidelines present updated information on the clinical and surgical management of RT for incorporation into clinical practice.

Patient summary: The European Association of Urology has released the renal transplantation guidelines. Implementation of minimally invasive surgery for organ retrieval and

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the latest evidence on transplant surgery as well as on immunosuppressive regimens are key to minimizing rejection and achieving long-term graft survival.

1. Introduction

This article represents the updated European Association of Urology (EAU) guidelines for renal transplant (RT) [1]. The main objective is to provide the urologists and kidney transplant (KT) surgeons practical guidance on the clinical management of RT focused on medical and surgical management. Clinical guidelines represent a summary of the highest evidence available to the experts; however, following the guidelines will not automatically result in the best outcome. Clinical guidelines can never replace the clinical and surgical expertise in the management of RT candidates, but these may help focus on decisions and take personal values and individual circumstances of patients into account.

2. Evidence acquisition

A broad and comprehensive literature search covering all sections of the RT guidelines was performed. Databases searched included Medline, EMBASE, and the Cochrane Libraries, covering a time frame between May 31, 2020 and April 1, 2023. For the 2024 RT guidelines, new and relevant evidence was identified, collated, and appraised through a structured assessment of the literature. For each recommendation within the guidelines, there is an accompanying online strength rating form that addresses a number of key elements:

1. The overall quality of the evidence that exists for the recommendation; references used in this text are graded according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence [2]
2. The magnitude of the effect (individual or combined effects)
3. The certainty of the results (precision, consistency, heterogeneity, and other statistical or study-related factors)
4. The balance between desirable and undesirable outcomes
5. The impact of patient values and preferences on the intervention

The strength of each recommendation is determined by the words "strong" or "weak" [3].

3. Organ retrieval and transplantation surgery

3.1. Living donor nephrectomy

There is strong evidence in support of laparoscopic living donor nephrectomy (LLDN), including several systematic reviews and meta-analyses, which have compared LLDN with open surgery [4]. Laparoendoscopic single-site surgery, and robotic and natural orifice transluminal endoscopic surgery–assisted living donor nephrectomy (LDN) should be performed only in highly specialized centers. LLDN is associated with similar rates of graft function and rejection, urological complications, and patient and graft survival. However, measures related to analgesic requirements, pain, hospital stay, and time to return to work are significantly better for laparoscopic procedures [5]. A recent meta-analysis comparing robot-assisted donor nephrectomy (RADN) and LLDN suggested that surgical experience enhances the perioperative outcomes following RADN more than it does following LLDN [6].

3.2. Organ preservation

In the absence of a cost-utility analysis, the results of the meta-analysis from the randomized controlled trials (RCTs) comparing University of Wisconsin preservation solutions with Celsior and Marshall's hypertonic citrate solution in standard cadaver donors indicate that these cold storage (CS) solutions are equivalent [7]. For living donors, in whom immediate KT is planned, perfusion with crystalloid solution is sufficient. Initial flushing with cold preservation solution followed by ice storage represents the standard method for kidney preservation. However, the limitations of static CS in preserving marginal organs such as expanded criteria donor (ECD) kidneys have led to the increased use of dynamic methods [8].

3.3. Methods of kidney preservation

The limitations of static CS in preserving marginal organs such as ECD kidneys have led to the increased use of dynamic methods.

A Cochrane systematic review and meta-analysis showed that hypothermic machine perfusion reduced the risk of delayed graft function (DGF) when compared with CS [9]. Moreover, mild hypothermia in ECDs whose organs are stored routinely using hypothermic machine perfusion might be associated with better kidney graft function after 1 yr after KT [10].

3.4. Donor kidney biopsies

Kidney discard in Europe is rarely based on histology findings [11]. Donor kidney biopsies can serve different purposes, including histological assessment of organ quality prior to transplantation and of focal lesions, especially if there is a suspicion of neoplasia. There is no consistent association between histological lesions observed in donor kidney biopsies and post-RT outcomes. Specifically, there is no agreement on prognostically relevant lesions and how they should be scored. Grading systems for donor kidney biopsies have not yet been developed, and lesion scoring in pre-RT biopsies is mostly based on the Banff consensus for post-RT renal allograft pathology, which is supported by the 2007 Banff Conference report [12]. An adequate biopsy

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reaches beyond the immediate subcapsular area (≥5 mm) and contains ≥25 glomeruli and one or more arteries. Paraffin histology employing special stains is technically superior to frozen sections since morphological details are better preserved on paraffin sections than on frozen sections [13].

Decisions on the acceptance of a donor organ should not be based on histological findings alone. Histology has to be evaluated in context with clinical parameters of the donor and recipient, including perfusion parameters where available [14].

Recently, a consensus document has been published on technical topics regarding a preimplantation biopsy in the process of ECD graft assessment that represents the first attempt in Europe to standardize procedures in this field [15].

3.5. Living and deceased donor implantation surgery

Preoperative hyperkalemia is the most common indication for preoperative hemodialysis, although its routine use is not indicated due to the potential to delay transplantation and increase cold ischemia time [16]. Based on low level of evidence, studies continuing antiplatelet therapy with aspirin, ticlopidine, or clopidogrel do not confer a significantly greater risk of peri/postoperative complications [17]. None of the current major thrombosis prevention guidelines directly address thromboprophylaxis in the RT perioperative period. Perioperative administration of short-acting anticoagulation agents reduces the perioperative risk of venous thrombosis (including in ileofemoral and renal veins); however, due to associated increased blood loss, administration requires knowledge of individual patient risk factors. A small RCT [18] showed no difference in early postoperative graft loss or thromboembolic complications with or without prophylactic anticoagulation.

Regarding antibiotic prophylaxis, it is strongly recommended to use single-dose, rather than multidose, perioperative prophylactic antibiotics in routine RT recipients [19].

Careful peri- and postoperative fluid balance is essential for optimal renal graft function. A small prospective RCT found that the use of Ringer's lactate solution was associated with less hyperkalemia and acidosis than normal saline in patients undergoing RT [20]. A small prospective RCT comparing constant infusion versus central venous pressure–based infusion (CVP) found that CVP produced a more stable hemodynamic profile, better diuresis, and early graft function [21]. Do not use low-dose dopaminergic agents routinely in the early postoperative period [22].

3.6. Surgical approaches for first, second, third, and further transplants

Transplant (bench/back-table) assessment and preparation before commencement of immunosuppression and induction of anesthesia are crucial steps in the transplantation process. Special attention has to be paid to exclusion of exophytic tumors, number, quality and integrity of renal vessels and ureter(s), and preservation of the peripelvic and proximal periureteral tissue (golden triangle). Open KT remains the standard surgical approach for the first or second single KT operations [23].

3.7. Specific technical recommendations

There is no evidence preferring the placement of a left or a right kidney into either iliac fossa [24].

Peri-iliac vessel lymphatics should be ligated to try and prevent postoperative lymphoceles. There is evidence supporting the benefits of cooling the kidney surface during implantation [25].

A recent registry study of 87 112 deceased donor kidney recipient pairs reported a modest increase in DGF and all-cause graft failure associated with the use of the right kidney, but there was no association with recipient mortality [26]. Nevertheless, the current evidence does not support declining an organ for KT based on laterality of the kidney offered [27].

The sites of the vascular anastomosis should be chosen carefully according to the length of the renal artery and vein to avoid kinking of the vessels when the kidney is placed into its final location, usually in the iliac fossa. A small RCT (n = 38) comparing end-to-end anastomosis to the internal iliac artery versus end-to-side anastomosis to the external iliac artery found that both techniques showed similar results in the early postoperative period and at 3-yr follow-up [28]. Lich-Gregoir–like extravesical ureterovesical anastomosis with a prophylactic ureteral stent is the elected technique to minimize urinary tract complications in RT recipients with normal urological anatomy (Table 1) [29].

In cases where an iliac artery prosthetic replacement has previously been carried out because of severe symptomatic iliac atheroma, the renal artery should be implanted into the prosthesis. Administration of systemic heparin should be considered prior to clamping of a vascular prosthesis [30].

In third or further transplants, the surgical approach must be planned preoperatively so that appropriate arterial

Table 1 – Recommendations and summary of evidence for single kidney transplant

Recommendation	SR
Use the external or common iliac arteries for an end-to-side arterial anastomosis to donor renal artery.	Weak
Use an end-to-end anastomosis to the internal iliac artery as an alternative to external or common iliac arteries.	Weak
Check the intima of the donor and recipient arteries prior to commencing the arterial anastomosis to ensure that there is no intimal rupture/flap. If this is found it must be repaired prior to/as part of the arterial anastomosis.	Strong
Preoperatively plan the surgical approach in third or further transplants, to ensure that appropriate arterial inflow and venous outflow exists with adequate space to implant the new kidney.	Strong
Summary of evidence	**LE**
A small RCT (n = 38) comparing end-to-end anastomosis to the internal iliac artery versus end-to-side anastomosis to the external iliac artery found that both techniques showed similar results in the postoperative period and at 3-yr follow-up.	1b
Cohort studies have demonstrated that third or further transplants are a valid therapeutic option with reasonable short- and long-term patient and graft survival.	3

LE = level of evidence; RCT = randomized controlled trial; SR = strength recommendation.

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inflow and venous outflow exist with adequate space to implant the new kidney. Nephrectomy of an old transplant kidney may be required prior to transplantation or at the time of transplantation, as well as mobilization of the common or internal iliac artery, internal iliac vein, or inferior vena cava. In some cases, an intraperitoneal approach (via the iliac fossa or midline) may be required. Rarely, orthotopic transplantation is needed [31].

Robot-assisted kidney transplant (RAKT) surgery is being evaluated in prospective nonrandomized trials (using the IDEAL consortium principles) [32].

Updated results in living donor RAKT report surgical and functional results competitive with open KT series [33]. Moreover, RAKT has been explored in orthotopic KT [34], cadaveric KT [35], and obese [36] patients, with preliminary promising results.

The rate of Clavien-Dindo grade III/IV complications is 3% after the first ten cases and the arterial graft thrombosis (1.6%) [37]. Patient and graft survival is 95% and 93% at 3 yr, respectively [36]. Evidence is too premature to recommend RAKT outside of appropriately mentored prospective studies.

4. Donor complications

A systematic review and meta-analysis on complications in minimally invasive LDN concluded that the techniques used for minimally invasive LDN are safe and associated with an overall complication rate of 16.8%. A meta-analysis found that obesity (body mass index >30) is associated with a significantly lower estimated glomerular filtration rate and higher blood pressure and proteinuria 1 yr after donation [38]. A study looking at the Norwegian Living Kidney Donor Registry found an increased long-term risk of ischemic heart disease in live kidney donors when compared with a healthy control group eligible to be donors [39].

The major Clavien classification of surgical complications of grade IV or higher affected 2.5% of donors. Risk factors for Clavien grade IV or higher events included obesity, predonation hematological and psychiatric conditions, and robotic nephrectomy. An annual center volume >50 was associated with a lower risk [40]. Survival rates and risk of end-stage renal disease are similar to those in the general population, while donors' health-related quality of life remains, on average, better than the general population.

It is highly recommended to restrict LDN to specialized centers and offer long-term follow-up to all living kidney donors.

5. Recipient complications

Arterial complications include thrombosis, stenosis, and arteriovenous fistula. The incidence or arterial thrombosis is low (0.5–3.5%) and usually is a consequence of a technical error during the anastomosis. The diagnosis depends on ultrasound (US) color Doppler followed by surgical exploration to assess the status of the graft. Thrombectomy in the case of a viable graft and allograft nephrectomy in the case a nonviable graft are the treatment options for renal artery thrombosis [41].

Arterial stenosis occurs in 1–25% of cases of RT. It is suspected in case of refractory arterial hypertension and/or increasing serum creatinine without hydronephrosis or infections. It is important to determine whether the stenosis is hemodynamically significant or not prior to treatment. Interventional radiology is the first-line treatment option; however, in patients considered unsuitable for radiological angioplasty, surgical treatment may be considered [42,43].

RT vein thrombosis is an early complication (prevalence 0.5–4%) and one of the most important causes of graft loss during the 1st postoperative month. The etiology includes technical errors and/or difficulties during surgery and the hypercoagulative state of the recipient. The diagnosis of renal vein thrombosis depends on color Doppler flow US followed by surgical exploration to assess the status of the graft. Thrombectomy in the case of a viable graft and allograft nephrectomy in the case a nonviable graft are the treatment options for renal vein thrombosis [41].

Lymphoceles occurs in 1–26% of RT. There is a significant etiological association with diabetes, mammalian target of rapamycin (m-TOR) inhibitor (ie, sirolimus) therapy, and acute rejection. Percutaneous drainage placement is the first treatment for large and symptomatic lymphoceles [44]. Surgical fenestration is recommended when percutaneous treatments fail.

The most important urinary complications are leak and stenosis. Urinary leakage occurs in 0–9.3% and is associated with failure and/or suture necrosis. Nontechnical risk factors include recipient age, number of renal arteries, site of arterial anastomosis, occurrence of acute rejection episodes, bladder problems, and immunosuppressive regimen. It should be suspected based on the urine output and the creatinine level in the drain fluid. For early and low-volume urine leaks, conservative management (JJ stent and bladder catheter and/or percutaneous nephrostomy) may be considered. When conservative management fails or massive urine leak occurs, surgical repair should be undertaken [45].

The incidence of ureteral stenosis is 0.6–10.5%. Early stenosis (within 3 mo of surgery) is usually caused by the surgical technique or compromised ureteral blood supply during surgery. Late stenosis (after >6 mo) is provoked by infection, fibrosis, progressive vascular disease, and/or rejection. Clinically significant ureteral stricture should be considered when persistent hydronephrosis occurs in association with impaired renal function. The first approach is the placement of a percutaneous nephrostomy tube with an antegrade pyelogram. Strictures <3 cm in length may be treated endoscopically. In case of strictures >3 cm in length or those that have reoccurred following a primary endourological approach, surgical reconstruction should be performed [46].

Kidney stones occur in 0.2–1.7% of RT [47]. Recommendations include a complete evaluation of the causes of urolithiasis in the recipient and management of ureteral obstruction due to a stone with a percutaneous nephrostomy tube or JJ stent placement. Treatment includes shockwave lithotripsy or antegrade/retrograde ureteroscopy for stones <15 mm and percutaneous nephrolithotomy for stones >20 mm (Table 2) [48]. Other complications include

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Table 2 – Recommendations and summary of evidence for complications after renal transplantation

Recommendation	SR
Perform ultrasound color Doppler in case of suspected graft arterial or venous thrombosis.	Strong
Perform ultrasound color Doppler to diagnose an arterial stenosis; in case of undetermined results on ultrasound, consider a magnetic resonance or computed tomography angiogram.	Strong
Perform percutaneous drainage placement as the first treatment for large and symptomatic lymphocele.	Strong
Manage urine leak by a JJ stent and bladder catheter and/or percutaneous nephrostomy tube. Perform surgical repair in cases of failure of conservative management.	Strong
Manage ureteral strictures <3 cm in length either with surgical reconstruction or endoscopically (percutaneous balloon dilation or antegrade flexible ureteroscopy and holmium laser incision). Treat late stricture recurrence and/or stricture >3 cm in length with surgical reconstruction in appropriate recipients.	Strong
Perform shockwave lithotripsy or antegrade/retrograde ureteroscopy for stones <15 mm.	Strong
Perform percutaneous nephrolithotomy for stones >20 mm.	Weak
Summary of evidence	**LE**
Thrombectomy in the case of a viable graft and allograft nephrectomy in the case a nonviable graft are the treatment options for renal artery thrombosis.	2b
Interventional radiology is the first-line treatment option for transplant renal artery stenosis; however, in patients considered unsuitable for radiological angioplasty, surgical treatment may be considered.	3
Surgical repair should be undertaken when conservative management fails or massive urine leak occurs.	2b
For strictures >3 cm in length or those that have reoccurred following a primary endourological Approach, surgical reconstruction should be performed.	2b
Extracorporeal shockwave lithotripsy should be considered as the first-line treatment option for stones <15 mm.	2b

LE = level of evidence; SR = strength recommendation.

hemorrhage, hematuria, reflux, acute pyelonephritis, wound infection, and incisional hernia [1].

6. Urological malignancy and RT

The risk of tumor recurrence was similar between transplantation and dialysis populations for renal cell carcinoma (RCC) and prostate cancer (PCa) [49].

Testicular cancer had a low risk of recurrence, but case reports highlighted the possibility of late recurrence even for stage I tumors [49].

For urothelial carcinoma, studies were mainly related to upper urinary tract carcinomas in the context of aristolochic acid nephropathy, for which the rate of synchronous bilateral tumors was 10–16% and the rate of contralateral recurrence was 31–39% [49].

These findings imply that a KT candidate with a history of appropriately treated low-stage/grade PCa (prostate-specific antigen $\leq$10, Gleason score $\leq$6, and T1/T2a) or low-grade T1 RCC could be listed for RT without any additional delay compared with a cancer-free patient. However, as the level of evidence was low, more studies are needed to standardize waiting.

In the potential donor kidney, the main surgical tumoral approach is ex vivo tumor excision on the back-table with an oncological margin, a frozen section biopsy, bench surgery renorrhaphy, and finally transplantation in the conventional fashion [50].

Treatment of localized PCa following KT is challenging due the presence of the kidney graft in the pelvic cavity close to the prostate. Surgery (radical prostatectomy) was the most frequently performed treatment for localized PCa (Table 3) [51].

7. Immunosuppression after KT

Increased understanding of immune rejection has led to the development of safe modern immune suppression agents, which suppress sensitized lymphocyte activity against a transplant. Immunosuppression is particularly important during the initial post-transplant period when there is a high incidence of early post-transplant rejection. Nonspecific side effects of immunosuppression include a higher risk of malignancy and infection, particularly opportunistic infections [52]. A multidrug regimen reflects the current standard of care for the majority of transplant recipients worldwide. It is strongly recommended to perform initial rejection prophylaxis with a combination therapy of a calcineurin inhibitor (CNI; preferably tacrolimus), mycophenolate (MPA), steroids, and an induction agent (either basiliximab or antithymocyte globulin) [53].

CNIs (cyclosporine and tacrolimus) are nephrotoxic, and their long-term use is an important cause of chronic allograft dysfunction, eventually leading to graft loss or severe chronic kidney disease in recipients of nonrenal organs. A meta-analysis of tacrolimus and cyclosporine has demonstrated similar outcomes to overall patient and graft survival [54]. Tacrolimus provided better rejection prophylaxis and was associated with better graft survival, when censored for death in some analyses. Renal function was favorable for tacrolimus-treated patients [55]. Owing to its higher efficacy, tacrolimus is recommended by current guidelines as first-line therapy [56].

MPAs (mycophenolate mofetil [MMF] or enteric-coated mycophenolate sodium [EC-MPS]) are based on mycophenolic acid, which inhibits inosine monophosphate dehydrogenase. Coadministration of MPA with prednisolone and a

Table 3 – Recommendations and summary of evidence for malignancy in renal transplant

Recommendation	SR
List for renal transplantation patients with a history of appropriately treated low-stage/grade renal cell carcinoma or prostate cancer without additional delay.	Weak
Do not discard a kidney for potential transplantation on the basis of a small renal mass alone.	Weak
Be aware of the presence of a kidney transplant in the pelvis and the possibility of subsequent transplants when planning treatment for prostate cancer.	Strong
Refer kidney transplant patients with prostate cancer to an integrated transplant urology center.	Strong
Summary of recommendations	**LE**
Overall 5-yr survival rates of renal cell carcinoma for transplantation vs dialyzed patients were 80–100% vs 76–100%.	2b
Overall, 1–5-yr survival rates of prostate cancer for transplantation patients ranged from 62% to 100%.	2b
Overall oncological outcomes following PCa treatment in kidney transplant recipients were comparable with those in the nontransplanted population.	2b

LE = level of evidence; PCa = prostate cancer; SR = strength recommendation.

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CNI has resulted in a profound reduction of biopsy-proven rejections [57]. Mycophenolic acid is not nephrotoxic; however, it inhibits bone marrow function and may cause cytomegalovirus (CMV) infections and gastrointestinal side effects [57]. There is also a higher incidence of polyoma nephropathy, especially when MPA is combined with tacrolimus [58]. Both MPA formulations, MMF and EC-MPS, are equally effective with an almost identical safety profile. Owing to a higher incidence of CMV disease with MPA, either CMV prophylaxis or a pre-emptive strategy with regular screening for CMV viremia should be instituted [58].

Azathioprine may be used in a low-risk population as an immunosuppressive drug, especially for those intolerant to MPA formulations [59].

Steroids have a large number of side effects, especially with long-term use. Most practitioners still consider steroids (either prednisolone or methylprednisolone) to be a fundamental adjunct to primary immunosuppression. Initial steroid therapy should be part of immunosuppression in the perioperative and early post-transplant period. Moreover, steroid withdrawal might be considered in standard immunological risk patients on combination therapy with a CNI and mycophenolic acid after the early post-transplant period [60].

The immunosuppressants sirolimus and everolimus inhibit m-TOR and suppress lymphocyte proliferation and differentiation. Mammalian target of rapamycin inhibitors exhibit dose-dependent bone marrow toxicity [61]. Other potential side effects include hyperlipidemia, edema, development of lymphoceles, wound-healing problems, pneumonitis, proteinuria, and impaired fertility [62]. Combination therapy with CNIs aggravates CNI-induced nephrotoxicity; CNI dosage should therefore be reduced substantially in combination therapy with m-TOR inhibitors, which seems to have no impact on efficacy, due to the highly synergistic potential of this combination therapy. Several studies suggest that m-TOR inhibitors cannot replace CNIs in the initial phase after transplantation due to lower efficacy and a less favorable side effect profile, particularly wound-healing problems and lymphoceles [61]. When combined with CNIs, antimicrobial prophylaxis for *Pneumocystis jirovecii* pneumonia should be administered for 1 yr following transplantation [63]. Conversion from CNIs is not advisable in patients with proteinuria >800 mg/d, and a cautious and individual approach should be followed in patients with a glomerular filtration rate of <30 ml/min [61]. Owing to an antiproliferative effect and a lower incidence of malignancy in m-TOR inhibitor–treated patients, conversion from CNIs to m-TOR inhibitors may be beneficial for patients who develop malignancy after transplantation or who are at a high risk of development of post-transplant malignancy or skin cancer [64].

Basiliximab, a high-affinity anti–interleukin-2 (anti–IL-2) receptor monoclonal antibody, is approved for rejection prophylaxis following organ transplantation. The drug is safe, and IL-2 receptor antibodies have been shown in RCTs to reduce the prevalence of acute cellular rejection by approximately 40%. Meta-analyses have confirmed the efficacy, although no positive effect on patient or graft survival could be demonstrated [65].

T-cell depleting antibodies may be used for induction therapy in immunologically high-risk patients. T-cell depleting antibodies may be used for induction therapy in immunologically high-risk patients [66]. Some centers use these agents to provide effective rejection prophylaxis while initiating CNIs after recovery of the graft from ischemic injury, although evidence supporting this hypothesis is lacking.

Belatacept (fusion protein, which effectively blocks the CD28 costimulatory pathway and thereby prevents T-cell activation) may be used for immunosuppressive therapy in immunologically low-risk patients, who have a positive Epstein-Barr virus serology [67].

8. Immunological complications

Immunological rejection is a common cause of early and late transplant dysfunction. There is great variation in the timing and severity of rejection episodes and how they respond to treatment. Today, two main types of immunological reactions are distinguished: T-cell–mediated rejections and antibody-mediated rejections [68]. The ultimate standard for the diagnosis of rejection is a transplant biopsy, because it is impossible to differentiate acute rejection based solely on clinical indicators from other causes of renal dysfunction (eg, acute tubular necrosis, infection, disease recurrence, or CNI nephrotoxicity). Therefore, all rejections should be verified by a renal biopsy, and biopsies should be classified according to the most recent Banff criteria [69]. There must be routine access to a US-guided biopsy of the transplant and sufficient expertise in the hospital pathology department to allow a rapid and clear-cut diagnosis of rejection or other type of allograft dysfunction. Moreover, steroid treatment for rejection may start before the renal biopsy is performed.

The use of steroid bolus therapy is strongly recommended as first-line treatment for T-cell–mediated rejection in addition to ensuring adequate baseline immunosuppression. In severe or steroid-resistant rejection, use intensified immunosuppression, high-dose steroid treatment, and eventually T-cell depleting agents. Treatment of antibody-mediated rejection should include antibody elimination [70].

9. Follow-up after transplantation

Regular long-term follow-up by experienced transplant physicians is essential in order to detect complications or graft dysfunction early and to reassure adherence to the immunosuppressive regimen [52]. Annual screening should include a dermatological examination, cardiovascular history and examination, tumor screening (including a nodal examination, fecal occult screening, chest x-ray, and gynecological and urological examination), and abdominal US, including US of the native and transplanted kidneys. If appropriate, further diagnostic tests should be prompted to treat or slow down the progression of any identified complication [71].

In patients diagnosed early with interstitial fibrosis and tubular atrophy, particularly if there is evidence for CNI tox-

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Table 4 – Recommendations and summary of evidence for follow-up after renal transplant

Recommendation	SR
Provide lifelong regular post-transplant follow-up by an experienced and trained RT specialist at least every 6–12 mo.	Strong
Advise patients on appropriate lifestyle changes, potential complications, and the importance of adherence to their immunosuppressive regimen.	Strong
Regularly monitor (approximately every 4–8 wk) serum creatinine, estimated glomerular filtration rate, blood pressure, urinary protein excretion, immunosuppression, and complications after RT. Changes in these parameters over time should trigger further diagnostic workup including renal biopsy, a search for infectious causes, and anti-HLA antibodies.	Strong
Perform ultrasound of the graft, in case of graft dysfunction, to rule out obstruction and renal artery stenosis.	Strong
In patients with interstitial fibrosis and tubular atrophy undergoing calcineurin inhibitor therapy and/or with histological signs suggestive of calcineurin inhibitor toxicity (eg, arteriolar hyalinosis, striped fibrosis), consider calcineurin inhibitor reduction or withdrawal.	Strong
Initiate appropriate medical treatment, eg, tight control of hypertension, diabetes, proteinuria, cardiac risk factors, infections, and other complications according to current guidelines.	Strong
Summary of recommendations	**LE**
Regular long-term follow-up by experienced transplant physicians is essential in order to detect complications or graft dysfunction early, and reassure adherence to the immunosuppressive regimen.	4
Annual screening should include a dermatological examination, cardiovascular history and exam, tumor screening (including a nodal examination, fecal occult screening, chest x-ray, gynecological and urological examination), and abdominal US, including US of the native and transplanted kidney. If appropriate, further diagnostic tests should be prompted to treat or slow down the progression of any identified complication.	4
In patients diagnosed early with IF/TA, particularly if there is evidence for CNI toxicity, disease progression may be slowed by conversion to a CNI-free regimen. If the risk of rejection seems too high, another option is substantial reduction of CNI under the protection of MPA.	1
Supportive measures should aim to adequately treat the consequences of chronic kidney disease (eg, anemia, acidosis, bone disease).	4

CNI = calcineurin inhibitor; IF = interstitial fibrosis; LE = level of evidence; MPA = mycophenolate; RT = renal transplant; SR = strength recommendation; TA = tubular atrophy; US = ultrasound.

icity, disease progression may be slowed by conversion to a CNI-free regimen. If the risk of rejection seems too high, another option is a substantial reduction of CNIs under the protection of MPA. Supportive measures should aim to adequately treat the consequences of chronic kidney disease (eg, anemia, acidosis, and bone disease; Table 4) [72].

10. Conclusions

These abridged EAU guidelines present updated information on the clinical and surgical management of RT for incorporation into clinical practice. Current evidence recommends pure or hand-assisted laparoscopic/retroperito neoscopic surgery as the preferential technique for LDN.

For organ preservation and CS, the use of either University of Wisconsin or histidine tryptophane ketoglutarate preservation solutions is recommended. Do not base decisions on the acceptance of a donor organ on histological findings alone, and optimize pre-, peri-, and postoperative hydration to improve renal graft function.

Perform a Lich-Gregoir–like extravesical ureterovesical anastomosis technique to minimize urinary tract complications in RT recipients with normal urological anatomy. It is also strongly recommended to restrict LDN to specialized centers and offer long-term follow-up to all living kidney donors.

Make a list of the RT patients with a history of appropriately treated low-stage/grade RCC or PCa without additional delay.

In the potential donor kidney, the main surgical tumoral approach is ex vivo tumor excision and finally transplantation.

Initial rejection prophylaxis comprises a combination therapy of a CNI (preferably tacrolimus), MPA, steroids, and an induction agent (either basiliximab or antithymocyte globulin).

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Study concept and design: Faba, Boissier, Budde, Figueiredo, Hevia, García, Regele, Zakri, Olsburgh, Breda.
Acquisition of data: Faba.
Analysis and interpretation of data: Faba, Breda.
Drafting of the manuscript: Faba, Breda.
Critical revision of the manuscript for important intellectual content: Faba, Boissier, Budde, Figueiredo, Hevia, García, Regele, Zakri, Olsburgh, Breda.
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