### Introduction

Kidney transplantation is the preferred treatment modality for kidney disease, and is associated with improved quality of life and survival compared to dialysis. But it is not a cure. For many patients, kidney transplantation provides more independence and allows them to return to normal life activities. Unfortunately, the demand for kidney transplants surpasses the supply of available organs, causing an increase in the number of patients on the waiting list, increase in the waiting time for a deceased donor transplant, and increase in the proportion of older adult patients undergoing kidney transplant. Preemptive kidney transplantation (transplant prior to dialysis) is the best option, but this only happens in a small percentage of patients with kidney failure and usually with an available living donor. Patients should not only understand the benefits and risks of transplantation, but also the responsibilities that followtransplantation related to self-monitoring, medications, financial issues, and their role in self-care.

Transplanted kidneys come from either the deceased donor waiting list or a living donor. Deceased donor kidneys are those from donors after death. All transplant centers operate under consistent regulations for offering deceased donor kidneys to waitlisted individuals. The allocation process considers both recipient factors (recipient age, current diagnosis of diabetes, time on dialysis) and donor factors (age of donor, cause of death, lab values, medical history). The kidneys are placed based on all these factors. This allocation process can also be explained in more detail to the patient by the transplant team (Organ Procurement and Transplantation Network, [OPTN], 2021).

Transplant centers will also consider kidneys from older deceased donors, donors with increased social risk behaviors, and/or those who are hepatitis B-or hepatitis C-positive. In certain scenarios, these kidneys are viable and able to be transplanted successfully.

The following is basic information about the transplantation process patients and their caregivers should consider carefully before embarking on the transplant process.

### **Transplant Evaluation/Candidacy**

Every transplant center has its own acceptance criteria for candidacy, protocol for evaluation, and absolute and relative contraindications. However, most centers agree on the major indications and contraindications for transplant, such as (Woodard & Zingraf, 2020):

- Current or recent malignancy, excluding noninvasive skin cancers.
- Active or chronic untreated infection.
- Untreatable heart or lung disease.
- Active substance abuse.
- Active untreated psychiatric illness/uncontrolled psychiatric condition.
- Unstable psychosocial situation that may lead to inadequate post-transplant care.

The transplant initial evaluation may include but is not limited to (Woodard & Zingraf, 2020):

- Initial consultation with the multidisciplinary team, including the transplant nurse/coordinator, transplant surgeon, transplant nephrologist or advanced practice provider, dietitian, pharmacist, social worker, and financial coordinator.
- Laboratory work: Blood and tissue type, screening for infectious diseases, clotting factors, screening for substance abuse.
- Diagnostic exams as indicated: chest X-ray, abdominal ultrasound, CT scan of iliac vessels, cardiac testing.
- Dental evaluation.
- Age-and gender-appropriate cancer screenings.
- Be current with all Centers for Disease Control and Prevention (CDC) recommended vaccinations.
- Any additional testing may be required by the transplant team based on the physical exam and medical history.

Kidney transplantation is an elective procedure — not an emergency or lifesaving. Therefore, patients should be in the best possible condition prior to transplantation. To achieve this, waitlisted patients should consistently follow their prescribed treatment regimen, avoid blood transfusions to decrease sensitizing events, and report major illnesses or hospitalizations as well as any contact information changes to the transplant center.

# Waiting List and Kidney Allocation of Deceased Donors

Once a patient has completed their full evaluation and has been approved for transplant by a multidisciplinary committee, they can be placed on the deceased donor waitlist via the United Network for Organ Sharing (UNOS). The average wait time for a kidney from a deceased donor varies across the country. Several factors determine the



Table 1.Blood Type Compatibility

Deceased Donor Blood Type	Is Compatible with Recipient Blood Type
A	A or AB
В	B or AB
AB	AB only
0	A, B, AB, or O

allocation of deceased donor kidneys. Some of these pertain to the deceased donor, some pertain to the candidate, and some are part of the OPTN policy regarding equitable allocation of kidneys. When a deceased donor kidney is available, a match run list of well-matched candidates is created. Elements used to develop that match run list include the following.

#### **Blood Type and Crossmatch**

Deceased donor kidneys are placed into a candidate on the waitlist with the same or a compatible blood type. The Rh factor is not relevant to this blood type matching (see Table 1).

Crossmatching is performed prior to a potential deceased donor transplant between a specific recipient and a specific deceased donor. Samples of blood are obtained from each and are mixed to see if the recipient's cells have a reaction to the donor's cells. If there is a reaction, that is called a POSITIVE crossmatch. The goal is for there to be no reaction (a NEGATIVE crossmatch).

#### **Waiting Time**

When a person is placed on the waiting list, they begin to accrue waiting time. This "wait time" is based on the following, per OPTN policies 8.3A and 8.3B (OPTN, 2022).

If a kidney candidate is 18 years or older on the date the candidate is registered on the waiting list, then the candidate's waiting time is based on the earliest of the following (OPTN, 2022).

- The candidate's registration date with a glomerular filtration rate (GFR) or measured or estimated creatinine clearance (CrCl) less than or equal to 20 mL/min.
- The date after registration that a candidate's GFR or measured or estimated CrCl becomes less than or equal to 20 mL/min.
- The date the candidate began regularly administered dialysis as a patient with end stage kidney disease

(ESRD) in a hospital based, independent non-hospital based, or home setting.

- If a kidney candidate is younger than 18 years at the time of registration on the waiting list, then the candidate's waiting time is based on the earlier of the following.
- The date that the candidate registered on the waiting list regardless of clinical criteria.
- The date that the candidate began regularly administered dialysis as an End Stage Renal Disease (ESRD) patient in a hospital based, independent non-hospital based, or home setting.

#### **Panel-Reactive Antibody (PRA)**

A panel-reactive antibody (PRA) is a group of antibodies in a test serum that are reactive against specific antigens in a panel of test leukocytes or purified HLA antigens from cells. The PRA is tested by the candidate's transplant center and is reported as a number between 0% and 100%. The higher the number, the more sensitized a candidate is, and the more likely they will have a positive crossmatch with a potential donor. If a person has had a prior sensitizing event, such as a pregnancy, blood transfusion, or prior transplant, they may have an elevated PRA. Those with a PRA of 98% to 100% are given priority in the allocation sequencing because they are the most difficult to match (higher incidence of a positive crossmatch with a donor).

#### **Kidney Donor Profile Index (KDPI) and Estimated Post-Transplant Survival (EPTS)**

Every kidney offered for a transplant has a KDPI score. This is a percentage score that ranges from 0% to 100%. The score is associated with how long the kidney is likely to function when compared to other kidneys. A KDPI score of 20% means the kidney is likely to function longer than 80% of other available kidneys. A KDPI score of 60% means that the kidney is likely to function longer than 40% of other available kidneys. (The healthier the kidney, the lower the KDPI score.)

The KDPI is calculated based on donor factors that affect how long the kidney is likely to function. These factors include:

- Age.
- Stroke as cause of death.
- Height.
- History of high blood pressure.
- Weight.
- History of diabetes.
- Ethnicity.
- Exposure to the hepatitis C virus.
- Whether the donor died due to loss of heart function or loss of brain function serum creatinine.

Figure 1.

#### Estimated Post-Transplant Survival (EPTS) and Kidney Donor Profile Index (KDPI)



Source: Organ Procurement and Transplant Network, 2023.

Each kidney candidate receives an individual EPTS score. This is a percentage score that ranges from 0% to 100%. The score is associated with how long the candidate will need a functioning kidney transplant when compared with other candidates. A person with an EPTS score of 20% is likely to need a kidney longer than 80% of other candidates. Someone with an EPTS score of 60% will likely need a kidney longer than 40% of other candidates. The younger and healthier the potential recipient is, the longer they can be expected to need a functioning transplant; therefore, the lower the EPTS score. The transplant team will calculate the EPTS score for each candidate based on these factors:

- Age.
- Length of time spent on dialysis.
- Having received a previous transplant (of any organ).
- Current diagnosis of diabetes mellitus.

How are KDPI and EPTS scores used in allocating kidneys? The 20% of kidneys expected to last the longest those with a KDPI score of 20% or less - are first offered to candidates likely to need a transplant the longest - those with an EPTS of 20% or less. If a kidney with a KDPI of 20% or less is not accepted for any of these candidates, it is then offered to any other person who would match, regardless of their EPTS score. Kidneys with high KDPI scores are expected to function for a shorter amount of time than others. They may be best used to help candidates who are less able to stay on dialysis for a long time. The 15% of donated kidneys likely to function the shortest time (those with a KDPI greater than 85%) will be offered first to a wider area of the country than other kidneys. The goal is to encourage use of these kidneys by finding a suitable candidate as quickly as possible.

#### **Other Factors**

Additional factors are considered with allocating kidneys from deceased donors:

- Pediatric kidney candidates (those under age 18 years).
- Previous living kidney donors.
- Candidates who meet medical urgency criteria.
- Proximity of candidates listed at transplant centers withing a 250 nautical mile radius of the donor hospital.

#### Keeping A Waitlisted Patient Ready for Transplant

It is hard to predict when a kidney will be offered to someone on the waiting list. Therefore, it is vital the patient always remains ready. When a patient is on the waiting list, it is important to report the following information to the transplant center:

- Up-to-date contact information for patient and caregiver.
- Records pertaining to any recent hospitalization, infection or illness.
- Non-compliance with dialysis, medications, or diet.
- Suspicion of substance abuse.
- Changes in social support system.
- Changes in insurance coverage.
- When the patient will be unreachable/unable to come in for a transplant.
- Up-to-date health maintenance (e.g., mammogram, PPD, dental, colonoscopy).
- Patient received a transplant at another center.
- Patient death.
- Communication between the patient/family, the dialysis unit or Chronic Kidney Disease (CKD) clinic, and the transplant center is vital to transplant success.

### **Living Donor Kidney Transplant**

A living kidney donor transplant is the best treatment for most people with kidney failure. Providing education about living transplants at CKD Stage 3 or 4 may allow time to plan and find a donor before the need for dialysis. A preemptive transplant and a living donor kidney provide the best outcomes and shorter waiting time. Unfortunately, no government-funded system is currently in place to help people find living donors like there is for deceased donor transplants. It is the responsibility of the recipient to find their own living kidney donor. Live donors may be related or unrelated to the recipient, and each transplant center has a process for live donor selection and evaluation in accordance with national regulations.

The following are several ways for someone to obtain a living donor kidney transplant.

<u>Directed donation</u> involves donating a kidney directly to a known compatible recipient.

**Paired donation** involves a donor who is not compatible with their intended recipient. They both are entered into a registry with other incompatible pairs. Using the registry computer program, donors and recipients are matched, allowing for compatible transplants to occur.

<u>Non-directed donation</u> involves donating a kidney directly to someone who is not known to the donor. This may also be called stranger, altruistic or Good Samaritan donation.

Kidney registries can create chains internally within a transplant center or through larger registries. Examples include the Alliance for Kidney Paired Donation (APKD), the National Kidney Registry (NKR), and UNOS Kidney Paired Exchange. It is not a requirement for transplant centers to be a member of a registry. However, being a member of a registry allows for a larger pool of donors and recipients, potentially providing an exchange of better matched kidney will last longer.

<u>Voucher donation</u> is an option for non-directed donors within kidney registries. Someone can donate a kidney to a stranger now and receive a voucher for a loved one to get a kidney in the future. There are several different types of vouchers, and not all registries or all transplant centers participate in voucher programs. It is important to ask transplant centers if they participate in either the APKD or NKR voucher program.

#### **Living Donor Selection and Care**

Living donors must be at least age 18 years, mentally sound with no suicidality. and have the capacity to make healthcare decisions. They should not feel pressure or obligation to donate, nor accept money for the donation. They must understand and consent to the short- and long-term risks.

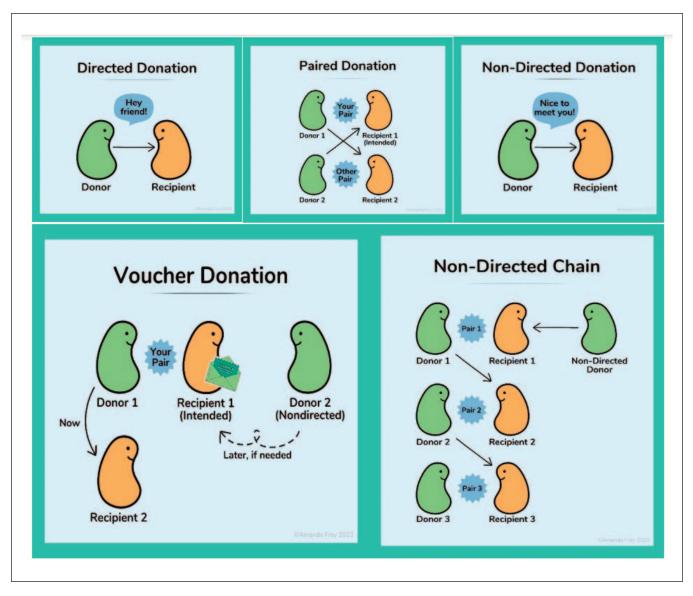
The medical evaluation minimally includes (OPTN 2023):

- Medical, family, and social history.
- Physical examination.
- Complete blood count, blood type, metabolic testing, pregnancy (must not be pregnant), chest X-ray, electrocardiogram.
- Testing for kidney function, stones, and anatomic assessment.
- Transmissible disease screening.
- Cancer screening.
- Additional testing may be needed, and each transplant center has policies for accepting or excluding donors.

Any living donor who is undergoing evaluation for donation must be provided with an Independent Living Donor Advocate (ILDA) who is not involved with the potential recipient evaluation (OPTN 2023). A donor nephrectomy requires a surgical procedure with general anesthesia. This may be done laparoscopically or through an open procedure, if necessary. Most donors have laparoscopic handassisted surgery that lasts around 4 hours. The usual hospital stay is one to three days. Follow-up visit with the surgeon is about two weeks after discharge. Driving is not recommended for two weeks and not while taking pain medications. Lifting is restricted to 10 pounds or less for six weeks. Full recovery is typically four to six weeks. Donors often return to work in two to four weeks, depending on the job. Pain medication and stool softeners may be prescribed after surgery. Follow up is required at six, 12, and 24 months, and donor status is reported to UNOS.

There is a slightly increased risk (15% to 20%) of developing high blood pressure long-term. There could be potential psychosocial problems (depression, stress, anxiety, etc.). Death rate is extremely low at 0.03% (3 in every 10,000 people who donate). Donors who become pregnant have an increased risk (5% compared to 2%) for preeclampsia, and careful monitoring is needed during the third trimester. The risk of kidney failure is the same as the general population.

Figure 2. Options for Obtaining a Living Donor Kidney Transplant



Source: Amanda Frey, 2023. Used with permission.

There is no charge to the donor for testing for workup, surgery, or initial post-op follow up. There may or may not be funds available to reimburse donor expenses, such as travel, lodging, meals, child care, and older adult care. Other donor protections may be available, depending on the state, kidney registry, or transplant center.

# Surgery and Postoperative Complications

Kidney transplantation is a well-established surgical procedure with an operative time of 4 to 6 hours. The kidney is transplanted into the recipient's iliac fossa. Advantages of

# Table 2. Classifications and Side Effects of Immunosuppressive Agents

Classification	Agent	Common Side Effects
Anti-inflammatory	Prednisone, methylprednisolone (Solumedrol®)	Altered fat deposition, cataracts, glaucoma, diabetes, hypertension, fluid retention, bone and muscle wasting, joint disease
Anti-proliferative	Azathioprine (Imuran®), mycophenolate mofetil (CellCept®), mycophenolic acid (Myfortic®)	Neutropenia, thrombocytopenia <b>Mycophenolate:</b> diarrhea, gastrointestinal intolerance, teratogenic
Calcineurin inhibitors	Cyclosporine modified (Neoral®), cyclosporine non-modified (Sandimmune®), Tacrolimus capsules (Prograf®), tacrolimus extended release capsules (Astagraf XL®), tacrolimus extended release tablets (Envarsus XR®)	Nephrotoxicity, diabetes, hypertension, hyperkalemia, tremors, neuropathies <b>Cyclosporine Modified:</b> Hirsutism, gingival hyperplasia
Antibody induction agents	Polyclonal antibody therapy: anti-thymocyte globulin (Thymoglobulin®) Monoclonal antibody therapy: basiliximab (Simulect®), alemtuzumab (Campath®)	Neutropenia, thrombocytopenia, bone marrow suppression
Mammalian target of rapamycin (mTOR) inhibitors	Sirolimus (Rapamune®), everolimus (Zortress®)	Hyperlipidemia, diarrhea, bone marrow suppression, delayed wound healing, mouth ulcers, proteinuria
T-cell costimulation blocker	Belatacept (Nulojix®)	Infusion-related reactions, anemia, post- transplant lymphoproliferative disease (PTLD) and other malignancies, progressive multifocal leukoencephalopathy (PML), rare

Sources: Colaneri & Neyhart, 2015; Danovitch, 2017.

iliac fossa placement are close location of the graft to the blood vessels and bladder, enhanced ability to assess the graft postoperatively, and ease of accessibility in the event of a biopsy or surgical intervention. Particular attention must be paid to potential complications, such as postoperative kidney function, impact of immunosuppressive therapy, and adjustment of patient and family to the transplant process. Assessment of kidney function requires diligent monitoring of urine quantity and quality, BUN, creatinine, and electrolytes.

Rejection continues to be one of the major problems of kidney transplantation. There are two primary causes of rejection. T cell-mediated (Cell mediated) and B cell-mediated (antibody-mediated, humoral).

<u>Hyperacute rejection</u>: Is rare, and typically manifests within minutes to hours after vascular anastomosis. It is humorally (antibody) mediated. Acute T cell-mediated (cellular) rejection (TCMR): Acute TCMR is due to cytotoxic T-cell reaction to HLA antigens on the donor kidney. These T cells can affect the tubules, interstitium, arteries, and even glomeruli. (Lusco et al., 2016). In one systematic review that included 12 studies of patients on tacrolimus and mycophenolate, the incidence of acute TCMR was 16% during the first posttransplant year. (Ho et al., 2022)

<u>Acute antibody-mediated rejection:</u> Typically occurs within the first few weeks to months post-transplantation and is a result of donor-specific antibodies (DSAs) that may be preformed (memory response) or may develop *de novo* (new antibodies).

Chronic allograft nephropathy (CAN): This is the most common cause of graft failure after one-year post-transplant. CAN may be rejection-related (cell-mediated or active antibody-mediated) or non-rejection-mediated (chronic hypertension, bacterial or viral infections, chronic obstruction, calcineurin Inhibitor [CNI] toxicity, nephrosclerosis, recurrent diseases).

Besides rejection, there are other types of transplant complications. These can be divided into post-transplant episodes (e.g., early and long-term complications) and infectious vs, noninfectious complications.

**Early complications** are those that occur during the first year after transplantation. These complications can be related to immunosuppression, rejection, infection, and technical problems related to the surgery. Some early post-transplant complications include delayed graft function (DGF), acute tubular necrosis (ATN), obstructive urethral problems, gastrointestinal effects, vascular, lymphatic, urologic, and wound-related.

Long-term complications following kidney transplant can be categorized as kidney allograft dysfunctions related to immunosuppressive therapy, cardiovascular diseases (CVD), hypertension, diabetes mellitus, hyperlipidemia, malignancy, metabolic, and psychosocial. Of these, the three most common causes of death in the late post-transplant period are CVD, infection, and malignancy.

### **Post-Transplant Medications**

Each transplant center has a protocol for induction, maintenance, and tapering of immunosuppressive agents. Table 2 outlines the most common anti-rejection agents and their side effect profiles.

### Transplantation: The Nurse's Role

Nephrology nurses working in subspecialties other than transplantation are in the unique position of having frequent contact with patients who may have an interest in kidney transplantation. While nurses who work in transplantation provide much of the transplant-related education, patients benefit greatly from regular discussions that may answer questions or clarify certain points. Nephrology nurses work across the spectrum of kidney disease in a variety of positions and settings: advanced practice providers, registered nurses, inpatient, outpatient, CKD clinics, and dialysis units. This gives them an opportunity to reinforce information related to transplantation and support their patients throughout the transplant process.

Information regarding kidney transplantation may be obtained through your local transplant centers, the United Network for Organ Sharing (UNOS), or the regional End Stage Renal Disease (ESRD) Network offices.

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### **ANNA Mission Statement**

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