Selection and Preparation of Kidney Transplant Recipient

The pre-transplantation evaluation is a multidisciplinary process that is performed well in advance of the renal transplantation operation & immune suppression. Evaluation for transplantation is a complex and time consuming process. A tremendous amount of information must be collected, reviewed, analysed, and synthesized in a cost effective manner.
The purposes of the evaluation are following:

To diagnose the primary renal disease and its risk of recurrence in the kidney graft.
To rule out active invasive infection.
To rule out a high probability of operating motality.
To assess compliance.
Top rule out active malignancy and
To whom it may concern, rule out unsuitable condition for technical success.

The pre-transplant evaluation usually takes place in an out-patient setting. A multi disciplinary team of transplant surgeons, nephrologists, nurses, social workers, nutritionists and financial coordinators form the core group that evaluated the patients. A transplant coordinator with expertise in the evaluation process coordinates the pretransplant evaluation. The main function of the transplant coordinator is to facilitate the referral consultation process, oversee the evaluation, present finding of the evaluation to the transplant team, and follow through with the team's recommendations.

PRELIMINARY SCREENING:

Initially preliminary information (i.e. information to determine financial feasibility) is collected from and shared with the patient and family (i.e. risks and benefits). In addition, attempts should be made to identify obvious barriers to transplantations such as ischemic heart disease or substance abuse.
Absolute and relative contraindications to kidney transplantations are listed in table.
Table: Contraindication to Kidney Transplantation

Contraindication	Absolute	Relative
Cancer	X	
HIV positive/ AIDS	X	
HCV Infections		X
HBV infection		X
Morbid obesity		X
Atherosclerosis		X
Cardiac Disease		X
Uncontrolled hypertension		X
Smoking		X
Unresolved psychosocial issues		X

Active UTI	X	
Active tuberculosis	X	
Irreversible heart failure	X	
Irreversible lung failure	X	
Irreversible liver failure	X	
Active systemic disease (i.e, lupus, sickle cell disease, Wegener's disease)	X	

The relevant issues which need a complete evaluation are:

KIDNEY DISEASE RECURRENCE:

Following diseases has risk of recurrence after transplantation

High risk of recurrence- Focal segmental glomerulosclerosis, haemolytic-uremic `syndrome, and primary oxalosis

Moderate risk of recurrence- Diabetes mellitus and IgA nephropathy

No risk of recurrence- Auto Somal Dominant polycystic kidney disease(ADPKD), renal dysplasia, and Alports Syndrome without antiglomerular basement membrane antibodies.

Infection

Infection must be detected and treated before transplantation or prevented with immunizations. Serologic testing for cytomegalovirus (CMV), human immune deficiency virus (HIV), Epstein-Barr virus, hepatitis B and C is mandatory. The treatment of chronic, active hepatitis B and C is evolving and patients with active hepatitis C infection may benefit from antiviral therapy before transplantation.

Unless the patient is protected by antibody development after infection or prior immunizations, the following immunizations are given to transplantation candidates: hepatitis A, hepatitis B, pneumococcus, diphtheria, tetanus, pertussis, polio, varicella, measles, mumps, and rubella.

Active Malignancy

A waiting time of 2 to 5 cancer-free years from the time of the last cancer treatment is recommended for patients who have had invasive malignancies, to reduce the risk of cancer recurrence. Shorter intervals from cancer treatment to transplantation are generally accepted for patients who have had low-grade, noninvasive cancers.

High Probability of Perioperative Morbidity or Mortality

Kidney transplantation candidates with a history of cardiac disease, cerebrovascular disease, or diabetes mellitus or who are older than 50year must undergo a cardiac performance evaluation.

Further testing and treatment are based on the results of a screening evaluation. It is recommended that patients older than age 50 year or with a history of coronary artery disease, cardiac symptoms, or insulin-dependent diabetes mellitus undergo stress cardiac testing with further diagnosis and treatment of significant cardiac disease before proceeding.
Cerebrovascular disease, peptic ulcer disease, and significant pulmonary disease must be detected and treated.
Cigarette smoking increases the risks of surgery, post-transplantation malignancy, cardiovascular disease, and renal allgraft loss. It must be stopped before transplantation in patients who already have clinical evidence of vasculopathy or cardiopulmonary disease.

Noncompliance

Compliance issue are extremely important in the long-term management of kidney transplant recipients. The transplant social worker and transplant coordinator collaborate to collect information related to cognitive, behavioural, and financial factors that will be either assets or liabilities to the candidate and the family and social issue that may affect medical outcomes; for example –information related to education, current and previous employment and occupations, disability status, substance abuse (current and past use of alcohol, drugs, or tobacco), activity level (ie, active or sedentary), and history of adherence to the medical prescriptions. Many centres have financial specialists who assist patients with insurance costs, medication coverage, and additional services is necessary to avoid a financial crisis later on.

Unsuitable Conditions for Technical Success

Evaluations of the vascular system and the urinary tract are necessary to identify probles that need to be corrected before transplantation or addressed at the time of transplantation.
Patients with symptoms and signs of lower extremity arterial disease or a history of abdominal or pelvic vascular surgery need to undergo a diagnostic evaluation to be certain that revascularization of a kidney graft is possible.
Vascular screening with Doppler flow studies and/or angiography may be required for correct vascular evaluation and/or treatment before transplantation.
Renal transplantation patients at risk for graft thrombosis are those with previous vascular access thrombosis, previous venous thrombosis, antiphospholipid antibodies, and previous large vein renal transplant thrombosis. Patients can be evaluated with the activated protein C- resistant ratio (factor V Leiden mutation), protein C activity, protein S activity, antithrombin III activity, homocysteine level, prothrombin gene mutation, and antiphospholipid antibodies.
The purposes of the urologic evaluation are to determine the suitability of the urinary bladder or its substitute for urinary tract reconstruction and to determine the necessity for removal of the native kidneys before or at the time of renal transplant. The urologic evaluation includes a history for urologic disease and operations on the urinary tract, a physical examination including the location of the scars, abdominal catheters, and stomas that may interfere with transplantation;

urinalysis; urine or bladder wash cluttering; and ultasonography of the abdomen and pelvis to include a postvoid bladder image, the kidneys, and the gall bladder.
Further study of the urinary tract is indicated for a history of urologic abnormalities, nonglomerular hematuria, single organism bacteriuria, calculi, hydronephrosis, ADPKD significant bladder residual urine, or inconclusive preliminary imaging studies.

The generally accepted indications for pretransplantations nephrectomy are outlined in

Table—Indications for Pretransplant Nephrectomy

1. Renal stones are not cleared by minimally invasive techniques or lithotripsy
2. Solid renal tumors with or without acquired renal cystic disease
3. Polycystic kidneys taht are symptomatic, extend below the iliac crest, have been infected, or have solid tumors
4. Significant proteinuria not controlled with medical nephrectomy or angioablation
5. Recurrent pyelonephritis
6. Grade 4 or 5 hydronephrosis

Guidelines For Kidney Transplantation – Living Donor Criteria

Living Kidney donation is accepted by law, religion and bioethics, provided that the donor is aware of the consequences of his/her act & makes the decision without outside pressure or commercialism.

Living donor evaluation includes a medical history, physical examination, laboratory tests, serologic screening & imaging studies in order to reach following conclusions:-

1. Donor has compatible blood and cross match with recipient.
2. Donor is healthy, with no unacceptable medical or surgical risk after donor nephrectomy.
3. Donor will have stable renal function after donation.
4. Donor does not have transmissible infection or malignancy.
5. Donor has an acceptable renal anatomy.
6. Donor does not have nor will have psychosocial problem.

In order to fulfill the above conclusion, following is the algorithm we follow:-

Psychosocial Evaluation

⇩

Blood compatibility *

⇩

Medical Evaluation

⇩

Surgical Evaluation

⇩

Consent

⇩

Donor Nephrectomy

⇩

Follow up

*** In select cases, the blood group barriers can be breached and mismatched blood group transplant can be undertaken**

The following reasons could exclude a living donor candidate from donating, based upon scientific data for medical risk, surgical risk, psychological assessment and/or consensus.

ABSOLUTE EXCLUSION CRITERIA

- Age <18 years
- Hypertension in someone younger than 50 years old, evidence of end organ damage, or on three or more anti-hypertensive medications
- Diabetes (diagnosis of diabetes) or abnormal glucose tolerance test
- History of thrombosis or embolism
- Psychiatric contraindications
- Obesity: BMI>35kg/m2
- Coronary Artery Disease symptomatic Valvular Disease
- Peripheral Vascular Disease
- Symptomatic Valvular Disease
- Chronic lung disease with impairment of oxygenation or ventilation
- Recent malignancy, or cancer with long times to reccurrence eg., breast cancer
- Significant Urologic abnormalities of donor kidney
- Proteinuria>300 mg/24hours
- HIV infection

RELATIVE CONTRAINDICATIONS:-

- Hepatitis C Virus Infection
- Hepatitis B Virus Infection
- Age 18-21 years old; elderly donors especially those without significant comorbid disease
- Obesity (BMI 30-35)
- Kidney stones
- Distant history of cancer
- Past history of psychiatric disorder
- Renovascular Disease
- Thin basement membrane disease
- Prior valve surgery
- Moderate Cardiac Valvular Disease with otherwise normal echocardiographic findings
- Mild sleep apnea without pulmonary hypertension

COMPATIBILITY OF DONOR

A well matched kidney from a live donor is one in which the blood type between the donor and recipient are compatible, the tissue typing well defined and hopefully well matched and with negative cross match studies. Thus, following are the recommendations for the blood compatibility:

- ABO blood group typing X2

- Human Leukocyte Antigen (HLA) typing
- Cross match

PSYCHOLOGICAL EVALUATION

A comprehensive psychiatric evaluation should be done to ensure that the prospective donor comprehends the risks, benefits and potential outcome of the donation for herself or himself and the recipient.

LIVING KIDNEY DONOR MEDICAL EVALUATION

A comprehensive medical evaluation of the donor is mandatory, in order to assess the surgical risk to him/her, to avoid immediate and long term morbidity. This includes:-

History

- Significant Medical History
- Surgical History
- Urological History _____
- Co Morbidities-

1. HTN _____ 2. CAD:_____

3. DM_____ 4. COPD:_____

Examination

1. GC _____ 2. Pulse_____

3. B.P_____ 4. Pallor_____

5. Icterus 6. Peripheral Edema

Abdominal Examination

1. Old scars
2. Hernial Site
3. External Genitalia
4. DRE

Investigation

Hematological

1.HB_____ 2. TLC_____

3. Platelets _____ 4. PT/APTT/INR _____

5. Serological Test for Infections:- HIV, HBsAG, HCV,CMV.

Urine Analysis

1. Urine R/E_____
2. Urine C/S_____

Biochemical

1. S.Creatinine_____
2. Na+_____
3. K+_____
4. Thyroid Function Test_____
5. Fasting Blood Sugar_____
6. Lipid profile_____

Imaging

1. USG KUB_____
2. X-ray KUB_____
3. CXR_____
4. ECG_____
5. ECHOCARDIOGRAPHY_____

Glomerular Filtration Rate Measurement

1.Creatinine clearance test_____
2. 24 hour urinary protein_____
3. DTPA For differential kidney function___

Cancer Screening

1. PAP for all women.
2. Mammogram for all women over 40 years or according to family risk.
3. PSA for all men over 50 years.
4. Colonoscopy for all donors over 50 Years old or younger according to family history (Preferable).

SURGICAL ANATOMIC EVALUATION

This includes the assessment of the anatomic features of the donor kidney to determine if nephrectomy can safely be performed, to determine which kidney should be removed & to determine what nephrectomy technique is to be employed.

For many years, Intra Venous Pyelography & renal angiography was used to evaluate renal anatomy, but now Spiral CT has replaced both IVP & MR.

The Left Kidney is preferentially selected for donation because of long left renal vein. The Right Kidney is selected for donation if:

- Left Kidney has more a complex vascular anatomy as compared to Right e.g. multiple vessels.
- Right kidney has only minor renal abnormalities like cyst, UPJ obstruction & left kidney is normal, especially in younger donors.
- In women who may become pregnant.

The kidney removal from a prospective kidney donor is either by an open approach or by a laparoscopic approach.

Whatever approach is used, following principles merit emphasis-:

- Donor safety at all times.
- Adequate exposure.
- Careful handling of the kidney, especially during periureteral dissection.
- Preservation of adequate perihilar & periureteral fat to ensure vascularity to ureter.
- Maintenance of active diuresis, which make prompt post transplantation function more likely.

INFORMED CONSENT

A fully informed consent of the potential living donor and exclusion of coercion and/or commercial practices are not only ethically necessary, but also mandated by most nations. Therefore, it is important to verify that the potential donor is acting voluntarily and altruistically and not under pressure or due to commercialism.

Donors should be made aware of the maximum level of risk that may incur, as well as the fact that they can change their mind at any point before operation.

LIVING DONOR FOLLOW-UP

After donation occurs, the transplant center must follow the living donor for two years. The donor may have the examinations at the center or may choose to visit another facility and have the evaluation results sent to the transplant centre.

Guidelines for Kidney Transplantation- Deceased Donor Criteria

Cadaveric Transplant involves removal of organs from a brain dead donor (DBD) with a functional circulation, or from patients with sudden cardiac death (DCD).

However, while the vast majority of organs are harvested from brain dead donors (DBD), the donor criteria pertain to both.

Most organ donors are victims of sudden illness or accident. The medical and nursing teams who have cared for the patient and assist the family also play a major role in obtaining permission for organ donation.

Notifying the Transplant centre as soon as possible helps ensure the best possible donor maintenance and permits more time for the identification of suitable recipients. Early notification allows the Transplant Centre to determine the suitability of the potential donor, even before the next of kin become finally committed to organ donation. It also helps in mobilizing the retrieval team and possible recipients in good time.

The criteria for an Deceased organ donor are:-

1. Normal Renal Function
2. No Hypertension Requiring Treatment
3. No Diabetes Mellitus
4. No Malignancy other than a primary brain tumor or treated superficial skin cancer
5. No Generalized viral or bacterial infection
6. Acceptable urinalysis
7. Negative assays for syphilis, hepatitis, HIV, & human T Lympho proliferative virus.

In order to meet the increasing demand of Cadaveric kidneys, some exceptions can be made in above listed criteria, resulting in the adoption of "Expanded Criteria Donors"(ECD).

ECD INCLUDES

- Donor less than 6 yrs of age
- Donor with age more than 60years; can be accepted if other parameters are normal.
- Donors 51 to59 years old with any two of the following risk factors
    - Cerebrovascular death
    - HTN
    - Serum Creatinine >1.5mg/dl

KIDNEY DONORS

Elevated Creatinine (up to 3 mg/dl) is not a contraindication, especially if the Creatinine level is falling and if the donor is known to have normal renal function in the recent past.

CONTRAINDICATIONS:-

- Chronic Renal Disease
- Age>70years; can be accepted if other parameters are normal.
- Potential metastasizing malignancy
- Severe Hypertension
- Current intravenous abuse
- HIV positive
- Oliguric Acute Renal Failure
- Untreated bacterial Sepsis
- Juvenile onset diabetes

*Apart from consent taken routinely from recipient, an additional informed consent must be taken for donors from Expanded Criteria.

Once the brain –dead donor is found to be within the criteria for organ donation, management is aimed at accomplishing the following goals:-

1. Maintenance of systolic BP of above 90 mm Hg with mean arterial pressure of 60 mmHG: give Hemaccel(or Normal Saline) rapidly, if BP fails to respond , initiate a Dopamine infusion(800mg in 500 ml of NS).

2. Maintain a urine output of >50ml/hour. If it can not be achieved with fluid replacement ,give 100ml of 20% mannitol or 100mg frusemide.

3. Maintain body temperature between 34° C & 36° C.

4. Insulin or/ and atropine may be required in presence of hyper glycemia & bradycardia respectively.

OPERATIVE AND RECOVERY PROCEDURES

The harvesting of the organs takes place at hospitals which have been licensed to do so by Appropriate Authority.

INTRAOPERATIVE DONOR MANAGEMENT

1. Maintain blood pressure, central venous pressure and urine output as previously described. Notify the surgeon of significant fluctuations.

2. Maintain a vigorous diuresis greater than 100 ml/hr immediately prior to aortic clamping. This may require 1-2 Liters of Ringer's Lactate for every hour that the abdomen is open.

3. The following drugs, provided by the recovery team, are administered via the i.v. infusion prior to hepatectomy at the request of the surgeon -300 units/ kg of body weight Heparin and 100 ml of 20% Mannitol.

POTENTIAL DONOR INFORMATION

When calling about a potential donor, the following information is very helpful:

DONOR HOSPITAL Tel No. Ward

ATTENDING

CONSULTANT

DONOR INFORMATION

Name:

Blood Group (including Rh):

Age: Sex:

Admission Diagnosis:

PAST MEDICAL HISTORY

? Renal disease
? Liver disease
? Hypertension
? Diabetes
? Alcholism
? Drug addiction
? Surgery

PAST MEDICAL HISTORY AND PHYSICAL STATUS

Temperature:
Ventilator:
BP:
Urine output: Last Hour:
Period of oliguria or anuria:
Episodes of cardiac arrest:
Other injuries:

Pulse:

Lowest Value:

Spontaneous respiration:
How long:
How long:
Catheter:
Last 24 hours:

CURRENT MEDICATIONS

Steroids
Antibiotics
Vasopressors
Transfusions
I.V fluids
Others

LABORATORY DATA

ABO Blood group: Blood Urea: S. creatinine:
Surface hepatits B Antigen (HBs Ag): HCV: HIV:
Liver function tests:
Bilirubin: SGPT:, SGOT: Aikaline phosphatase:
Blood gases:
pH: PCO 2: ,PO 2: Bicarb:
Total CO 2: Base excess:

Electrolytes:
Microbiological data:

HAS THE DIAGNOSIS OF BRAIN DEATH BEEN ENTERTAINED?

Yes / No Time
Family approached? Yes /No
Permission granted? Yes / No

TISSUE TYPING is carried out on peripherial sample of blood. To confirm the blood group, 10ml of donor blood collected in a plain vial is required in all cases.

History of Renal Transplantation

Transplantation of kidney for treatment of renal failure has been an attractive concept for many years.

Interest in modern transplantation developed in the early part of 20th century because of innovation in experimental & clinical surgical skills. Payr's demonstrated the first workable method of vascular suturing that led to widespread interest in organ transplantation.

In Vienna, Ullmann & Alfred Von Decastello were first to report a successful experimental organ transplant, using Payr's method of vascular suturing, in 1902.

Ullman managed to auto transplant a dog kidney from its normal position to the vessels of the neck and Von Decastello had carried out dog to dog kidney transplants.

In Lyon, Mathieu Jaboulay (1860-1913), along with Carrel, who had worked on improvement of vascular suturing, carried out first xenograft kidney transplant using pigs and goats as donor, transplanting the organ to the arm or thigh of patient with ESRD.

Soviet surgeon Yo-Yo Vorony performed first allograft human kidney transplant, transplanting kidney from a patient dying of head injury to the thigh vessels of recipient. The kidney did not work but post-mortem suggested patent donor vessels. In this era of first half of 20th century, it was now evident that although surgically organ transplantation is possible, but the organ were not be able to function. Thus simultaneous efforts were started in order to achieve proper function of the transplanted organ.

Dempstein, in London, and Simonsen, in Denmark, found that pelvic position of kidney was preferable to superficial site & also concluded that an immunological factor was the cause of failure in earlier allograft transplants.

In early 1950, various centres in Europe & USA had attempted renal allograft transplant but with a very little success.

The first kidney transplants between living patients were undertaken in 1954 in Boston and Paris. The Boston transplantations, performed on December 23,1954, at Brigham Hospital was performed by Joseph Murray, J. Hartwell Harrison, John P. Merill and others. The procedure was done between identical twins, to eliminate any problems of an immune reaction. For this and later work, Dr. Murray received the Nobel Prize for Medicine in 1990. The recipient died eight years after the transplantation.

There still remained the apparently almost insoluble problem of rejection of any kidney other than an identical twin kidney.

The first attempt to suppress the immune response was total body irradiation of recipient carried out by Dr. Merril's group in Boston, Dr. Kuss & Dr. Hamburger in Paris & by Proff. Shackmans group in London. But radiation was associated with unacceptable complications.

Then came the discovery of 6 Mercaptopurine by Dr. Schwartz and Dameshek in 1959, which was the first light of emerging immune suppressants.

This is followed by introduction of Azathioprine in 1960 in New York & with addition of steroids; the standard immune suppressive therapy of today was introduced to the practice of renal transplantation in early sixties.

This was followed by, the clinical use of Cyclosporine in 1978 & of Tacrolimus in 1987. Simultaneous work on tissue typing had also contributed for long lasting success of transplant. First noted by Terasaki & associates it was described in more detail by Kissmeyer Niclson & coll. In 1966, Pre-transplant cross match between donor cells & recipient serum had led to a marked diminution in hyperacute rejection.