CKD MANAGEMENT In TERTIARY CENTER

Prof. Thu Zar Thin
Renal Medical Ward
Thingungyun General Hospital
(500 Bedded)

22.01.18

Outlines

1. Level of Care
2. CKD definition
3. At – Risk population
4. Aggravating Factors
5. Treatments slow the progression of CKD
6. Important of Early Referral of CKD patients
7. RRT modalities
8. KT evaluation

LEVELS of CARE

- Medical professionals frequently talk about levels of care
  (1) Primary care
  (2) Secondary care
  (3) Tertiary care
  (4) Quaternary care

- Related to the complexity = medical cases being treated as well
  = the skills and specialties of the provider

Primary Care Essentials

- Primary care doctor = A new symptom or
  A cold, the flu, or
  Some other bacterial or viral disease or
  A broken bone, a sore muscle,
  a skin rash, or
  Any Acute Medical Problem

- Primary care = Typically responsible for coordinating your care among specialists and other levels of care

- Primary care providers (PCPs) = Doctors, nurse practitioners, or physician assistants

- Primary care "specialties" (to specialize in caring for a particular group of people)
  - = OB-GYNs
  - = Geriatricians
  - = Pediatricians

Secondary Care Specialists

- Primary care provider refers
  = A specialist → secondary care

- Secondary care
  = Care of by someone who has more specific expertise
  = Cardiologists, Endocrinologists and

Tertiary Care and Hospitalization

- Once a patient is hospitalized and needs a higher level of specialty care within the hospital → referred to "tertiary care"

- Tertiary care
  = Requires highly specialized equipment and expertise

- Renal or hemodialysis, Acute Coronary Bypass Surgery and some plastic surgeries or neurosurgeries

Quaternary Care

- An extension of tertiary care
- More specialized and highly unusual, More specific
- Only offer quaternary care for particular medical conditions or systems of the body
- Interventionist

Definition of Chronic kidney disease

Chronic kidney disease is defined as:

Glomerular Filtration Rate (GFR) < 60 mL/min/1.73m^2 for ≥3 months with or without evidence of kidney damage

Evidence of kidney damage (with or without decreased GFR) for ≥3 months:

- Albuminuria
- Haematuria after exclusion of urological causes
- Pathological abnormalities
- Anatomical abnormalities

Stage	eGFR ml/min/1.73m^2	Description
1	90+	Normal kidney function but urine findings or structural abnormalities or genetic trait point to kidney disease
2	60-89	Mildly reduced kidney function and other findings point to kidney disease as for stage 1
3A	45-59	Moderately reduced kidney function
3B	30-44	Moderately reduced kidney function
4	15-29	Severely reduced kidney function
5	<15 or on dialysis	Very severe or end stage kidney failure

TABLE 16-1. Staging System and Action Plan for Chronic Kidney Disease

STAGE	DESCRIPTION	GFR (mL/min/1.73 m²)	ACTION*
0	At increased risk of CKD	≥90 with risk factors†	Screening CKD risk reduction
1	Kidney damage with normal or increased GFR†	≥90	Diagnosis and treatment Slow progression of CKD Treat comorbidities Cardiovascular disease risk reduction
2	Mild decrease in GFR	60 to 89	Estimate progression
3A	Mild to moderate decrease in GFR	44 to 59	Evaluate and treat complications
3B	Moderate to severe decrease in GFR	30 to 44	Treat complications Initiate discussions about options for possible future need for renal replacement therapy
4	Severe decrease in GFR	15 to 29	Treat complications Prepare for RRT
5	Kidney failure	<15 or dialysis	Renal replacement if uremic or other indications present

*Includes actions from preceding stages.

Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m^2) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

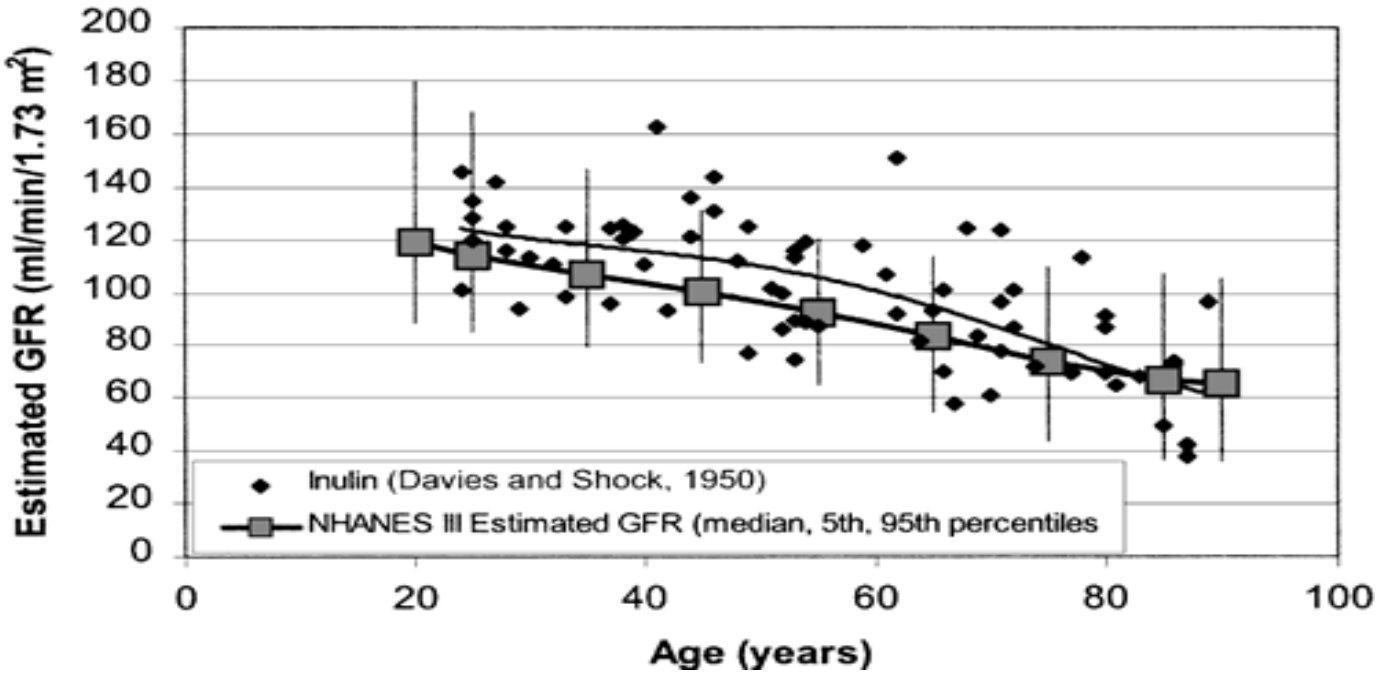
- Prevalence
- Causes
- At - Risks Population

Risk Factors associated with Initiation and Progression of Chronic Kidney Disease

INITIATION FACTORS	PROGRESSION FACTORS
Systemic hypertension Diabetes mellitus Cardiovascular disease Obesity/metabolic syndrome Hyperuricemia Smoking Low socioeconomic status Nephrotoxins (NSAIDs, analgesics, herbal supplements, heavy metals, etc)	Older age Male gender Race/ethnicity Genetic predisposition Poor blood pressure control Poor glucose control Proteinuria Cardiovascular disease Dyslipidemia, smoking, obesity/metabolic syndrome, hyperuricemia, low socioeconomic status ETOH consumption, nephrotoxins (NSAIDs, analgesics, herbal supplements, contrast material, etc) Acute kidney injury

GFR

- The normal annual mean decline in GFR with age from the peak GFR (~120 mL/min per 1.73 m^2) attained during the third decade of life is ~1 mL/min per year per 1.73 m^2,
- Reaching a mean value of 70 mL/min per 1.73 m^2 at age 70.



Early & Effective T/M of Cause

1. Glomerular diseases = Specific IS
2. Diabetes = Tight control in early stage (? Late stage)
3. Hypertension
4. Obstruction = stone (? Prevention)
5. Hyperuricaemia
6. Urinary tract infection
7. Analgesic nephropathy

Factors that increase the risk to develop diabetic nephropathy (modifiable)

Hyperglycaemia

Smoking

Hypertension

High protein intake?

Dyslipidaemia?

- primary prevention & secondary prevention of DN

Interventions in overt diabetic nephropathy

Factors that increase the risk of progression of diabetic nephropathy to ESRD

Hypertension

Proteinuria

Smoking

Poor glycaemic control

Dyslipidaemia?

High dietary intake of protein?

REMOVING THE AGGRAVATING FACTORS

1. Fluid & Electrolyte imbalance
    (a) Dehydration
    (b) Sodium deficit/ HyperNa
    (c) Hypokalaemia/HyperNa

2. Haemodynamic disturbance
    (a) Congestive heart failure
    (b) Hypotension
    (c) Shock

3. Hypertension especially malignant

4. Urinary tract infection

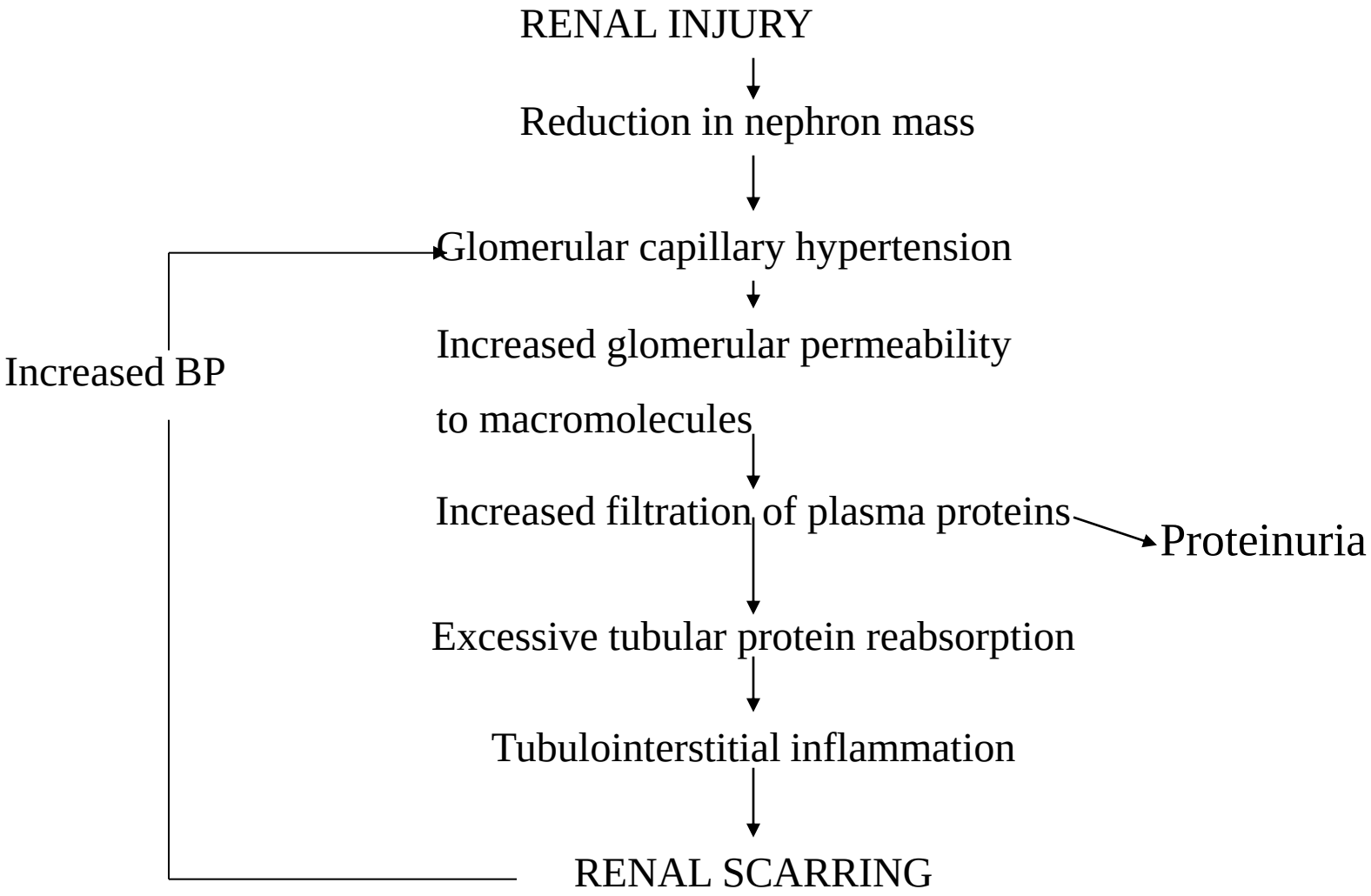
5. Nephrotoxins
   (a) Aminoglycosides
   (b) Tetracycline
   (c) N.S.A.I.D
   (d) Radio contrast material
   (e) Indigenous medicines

6. Metabolic disorders
   (a) Hypercalcaemia
   (b) Hyperphosphataemia
   (c) Hyperuricaemia
   (d) Hyperoxaluria

7.Urinary tract obstruction

PROGRESSIVE RENAL DAMAGE:

The Final Common Pathway



- Treatment of chronic kidney disease (CKD) can slow its progression to end-stage renal disease (ESRD)

- Therapies - limited role

- The rate of progression of CKD to end stage renal disease (ESRD) can be reduced by the early detection and Mx of risk factors and complications associated with it

Blood Pressure Control

- In general, optimum blood pressure control (< 140/90) reduces renal disease progression and cardiovascular morbidity and mortality

- The 2013 KDIGO guidelines on CKD and blood pressure control state the following blood pressure goals for patients with CKD:

Urine Albumin Excretion	Blood Pressure Goal
< 30mg/24 hours	< 140/90 (recommended)
> 30mg/24 hours	< 130/80 (suggested)

- Antihypertensive agents,
  ACEIs and ARBs are particularly effective in slowing disease progression in both diabetic and non-diabetic CKD

- If ACEI or ARB is not effective on its own to control BP,
  Thiazide or dihydropyridine calcium channel blocker (e.g., amlodipine) may be added

- Dihydropyridine calcium channel blockers should not be prescribed without the concomitant usage of ACEI or ARB, since their sole use may lead to greater hyperfiltration and albuminuria.

Management of Comorbid Conditions

- Common comorbid conditions among patients with CKD include diabetes, cardiovascular disease, and hyperlipidemia

- Managing these comorbid conditions aggressively is important

- Suboptimal control of these secondary conditions increases the risk for progression of CKD

- Additionally, the presence of CKD increase risk of morbidity and mortality associated with the comorbid conditions themselves.

Diabetes mellitus

- Relatively strict control of blood glucose (hemoglobin A1C ≤7%) in both type 1 and type 2 diabetes reduces the development of diabetic nephropathy and its progression.

- HbA1c may not be truly accurate (falsely low as a result of decreased red blood cell [RBC] lifespan, transfusions, and hemolysis) in CKD patients

- Research efforts are focused on glycated albumin as a measure of diabetic control in those with advanced stages of CKD.

Preferred antihypertensive therapy among diabetics with hypertension would be an ACEI or an ARB. While no evidence supports use of RAAS therapy among normotensive normoalbuminuric patients with diabetes, ACEI or ARB therapy is recommended among normotensive diabetics with microalbuminuria.

Due to the high incidence of CKD among patients with diabetes, annual surveillance for CKD using serum creatinine and urine microalbumin to creatinine ratio is recommended for this patient population.

Dietary protein restriction

- Effects on renal haemodynamics →↑ GFR and renal plasma flow
  → prostaglandins or glucagon
  → not vegetable sources

- Recommend - intake of 0.8 g/kg body weight / day

- The small effect < lowering of BP and ACE inhibitors

- We suggest avoiding high protein intake (>1.3 g/kg/day) in adults with CKD at risk of progression. (2C)

LIPID LOWERING

- Observational studies in humans suggest that reducing serum lipid levels is associated with preservation of kidney function
  = small patient numbers

- A meta analysis of 13 studies revealed a trend toward reduction in proteinuria and a small decrease rate of GFR loss with lipid lowering

- Two large scale RCTs
  (Prevention of Renal and Vascular End-stage Disease
  Intervention Trial [PREVEND-IT] and
  (European Study for Preventing by Lipid-lowering Agents
  and ACE-inhibition Dialysis Endpoints (ESPLANADE)
  = failed to show a beneficial effect of statins on albuminuria
  in patients who were treated with ARBs

- The SHARP(Study of Heart and Renal Protection) study
  = A randomized, prospective, controlled trial examining the combination of ezetimibe and simvastatin,
  = All-cause and cardiovascular mortality were not improved

- Combination therapy did not decrease the risk of progression to ESRD in CKD patients who were not on dialysis at baseline, as compared with placebo

Smoking

- Smoking aggravates the excessive cardiovascular risk in CKD patients

- A random sample of new ESRD patients in the United States noted that smokers had a 22% greater risk of developing coronary artery disease

- smoking cessation is an important preventive intervention

KDIGO Recommended Statin Dosing in Adults with CKD

Table 10. Statin/Lipid Treatment in Patients with CKD

CKD Patient Population	Treatment
Age ≥ 50 years with eGFR < 60 ml/min/1.73 m2 and no previous kidney transplant (G3a-G5)	Statin or statin + ezetimibe [1]
Age ≥ 50 years with eGFR ≥ 60 ml/min/1.73 m2 (G1-G2)	Statin
Age 18-49 with eGFR ≥ 60 ml/min/1.73 m2 (G1-G2) and either: known coronary disease (myocardial infarction or coronary revascularization), diabetes mellitus, prior ischemic stroke, or estimated 10-year incidence of coronary death or non-fatal myocardial infarction > 10% [2]	Statin
Transplant recipient (adult any age)	Statin
Hypertriglyceridemia	Therapeutic lifestyle changes

Note: Adapted from the KDIGO Clinical Practice Guideline for Lipid Management in Chronic Kidney Disease, 2013.

[1] Option to add ezetemibe is based on the SHARP (Study of Heart and Renal Protection) trial.

[2] Calculators to estimate 10-year incidence of coronary death or non-fatal myocardial infarction include: Framingham risk score, Reynold's, SCORE, PROCAM, ASSIGN, or QRISK2.

Table 14. Key Elements of Patient Education for CKD

Elements

- Ensure patient awareness of CKD diagnosis
- "Know your numbers"- make patients aware of their kidney function (eGFR and creatinine) and blood pressure goals
- Provide familiarity with the need for screening and treatment of comorbid conditions (e.g., diabetes, hypertension, CAD)
- Instruct patients to avoid potentially nephrotoxic OTC medications, especially NSAIDS, herbal medications, unsupervised use of vitamin and minerals or nutritional protein supplements
- Encourage patients to talk with their primary care physician, nephrologist or pharmacist before starting new medications to ensure safety and appropriate renal dosing
- Promote lifestyle modifications
    - Diet, with special attention to sodium, potassium and phosphorus intake
    - Regular exercise
    - Maintain a healthy body weight
    - Immunizations
    - Tobacco cessation

Resources

Patient education resources are available at the National Kidney Foundation Website (kidney.org/)
For links to recommended patient education materials, visit the University of Michigan Clinical Care Guidelines website

Drug-Induced Nephrotoxicity: Prevention Strategies, Patient Risk Factors, and Associated Drugs

General Strategies to Prevent Drug-Induced Nephrotoxicity

Assess baseline renal function prior to initiating potentially nephrotoxic drugs
Adjust medication dosages based on renal function as needed
Avoid nephrotoxic drug combinations
Use non-nephrotoxic alternatives whenever possible
Correct risk factors for nephrotoxicity before initiating drug therapy whenever possible
Ensure adequate hydration before and during therapy with potential nephrotoxic drugs
Limit dose and duration of therapy when possible

Key Risk Factors Predisposing Patients to Drug-Induced Nephrotoxicity

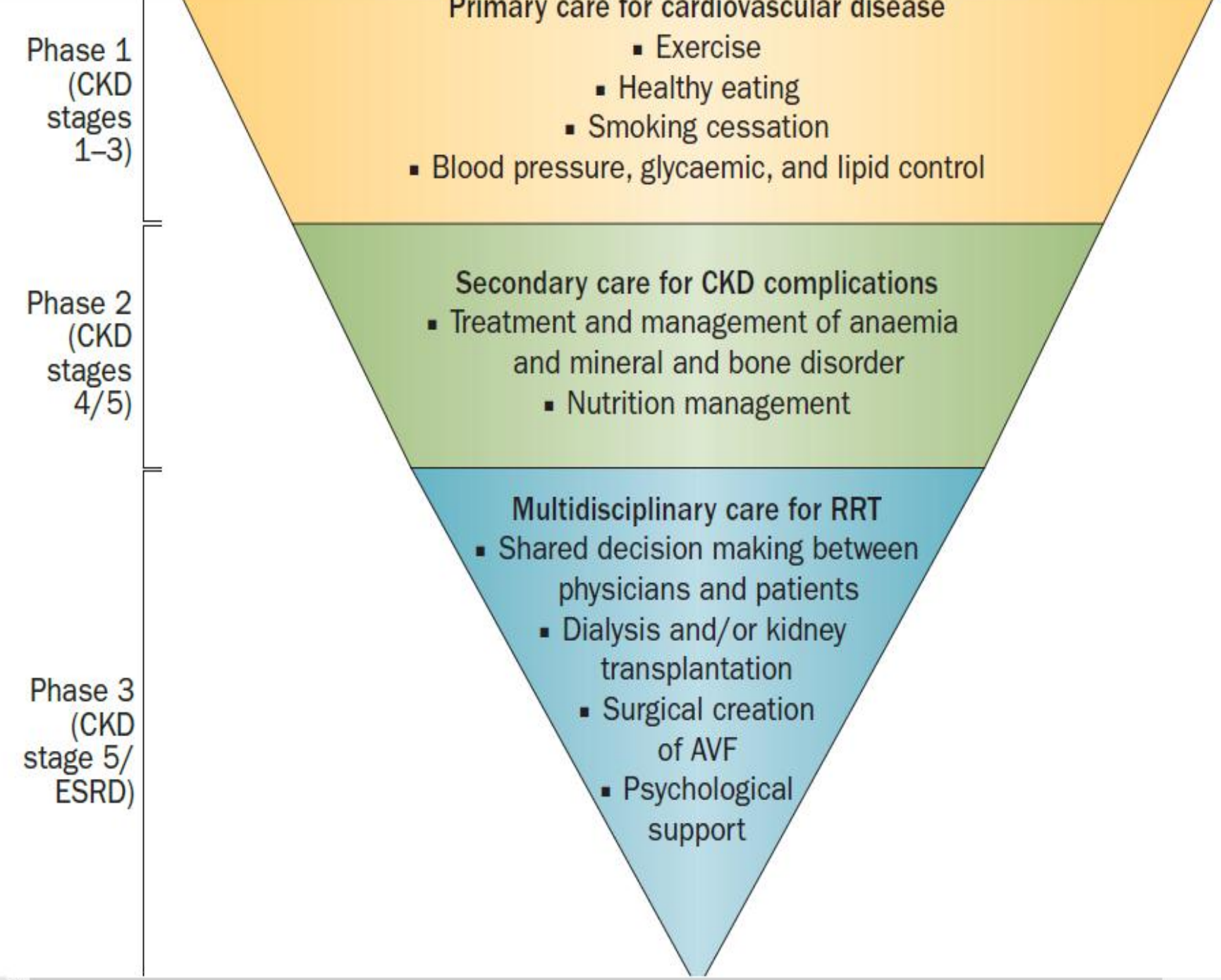
Key Risk Factors Predisposing Patients to Drug-Induced Nephrotoxicity

Age greater than 60 years
Diabetes mellitus
Drug-drug interactions resulting in synergistic nephrotoxic effects
Exposure to multiple or high doses of nephrotoxins
Heart failure
History of kidney transplant
Multiple myeloma
Sepsis
Underlying kidney dysfunction (e.g., eGFR < 60 mL/min, renal artery stenosis)
Vascular disease
Volume depletion

Heart failure	Volume depletion
History of kidney transplant	

Select Drugs Associated with Nephrotoxicity	
Allopurinol	Lithium
Aldosterone inhibitors	Loop diuretics
Angiotensin-converting enzyme inhibitors	Methamphetamines
Angiotensin II receptor blockers	Methotrexate
Calcium channel blockers	Nonsteroidal anti-inflammatory drugs
Cephalosporins	Oral sodium phosphate solution
Combined phenacetin, aspirin, and caffeine analgesics	Pamidronate
Cyclooxygenase-2 inhibitors	Penicillamine
Cyclosporine	Penicillins
Digoxin	Propylthiouracil
Direct renin inhibitors	Proton pump inhibitors
Fluoroquinolones	Iodinated contrast agents
Foscarnet	Rifampin
Gold	Sulfonamides
Hydralazine	Tacrolimus

Note: See Tables 18 and 19 for drugs, natural products, and herbs that may affect CKD patients.


Phase 1 (CKD stages 1–3)
Primary care for cardiovascular disease
▪ Exercise
▪ Healthy eating
▪ Smoking cessation
▪ Blood pressure, glycaemic, and lipid control
Phase 2 (CKD stages 4/5)
Secondary care for CKD complications
▪ Treatment and management of anaemia and mineral and bone disorder
▪ Nutrition management
Phase 3 (CKD stage 5/ ESRD)
Multidisciplinary care for RRT
▪ Shared decision making between physicians and patients
▪ Dialysis and/or kidney transplantation
▪ Surgical creation of AVF
▪ Psychological support

PREPARATION OF THE CHRONIC KIDNEY DISEASE PATIENT FOR RENAL REPLACEMENT THERAPY

- A critical part of CKD care → preparation of patients
  - = Emotional
  - = Physical

- Evaluation and management of the patient with advanced CKD

- Preparation for RRT

Treatment Options for CKD

I. Renal Replacement Therapy

(1) CAPD (Continous Ambulatory Peritoneal Dialysis)

(2) Hemodialysis

(3) Renal Transplantation

II. Conservative Treatment

- Improved predialysis care = Reduces the mortality rate

- Appropriate timing of nephrology referral
- ESRD preparatory care
- Critical components of patient education
- Resources availablility
- Optimal time of RRT initiation

- A major reason for this problem is late referral (1 to 4 months prior to RRT) of CKD patients to nephrologists

- Late referral is associated with increased morbidity

- A graded risk reduction for patient mortality is noted with early referral (>12 months)

Consequences of Late Referral

Severe metabolic acidosis

Severe hyperphosphatemia

Marked anemia

Hypoalbuminemia

Severe hypertension and volume overload

Low prevalence of permanent dialysis access

Delayed referral for renal transplantation

Higher initial hospitalization rate

Higher costs of initiation of dialysis

Increased 1-year mortality rate

Decreased patient choice in RRT modality selection

Benefits of Early Referral to Nephrologist

Improved vocational outcomes

Delay in need to initiate RRT

Increased proportion of patients with permanent vascular access, particularly AVF > AVG (arteriovenous graft)

Patient modality selection differences—greater peritoneal dialysis usage

Reduced need for urgent dialysis

Reduced hospital length of stay and health care costs

Better metabolic parameters at dialysis initiation

Better patient survival

- **Reasons for Late referral**
  = Economic barriers (ie, lack of insurance)
  = patient factors (denial, fear, and procrastination)
  = Provider factors
    - Under appreciation of severity of disease
    - Fear of alarming the patient
    - Lack of a multidisciplinary care team
    - Inadequate frequency of patient follow up
    - Lack of training about both the appropriate timing and indications for referral of CKD patients to
    - Poor communication and feedback from nephrologists following CKD patients

- The National Institutes of Health (NIH) Consensus Development Conference Panel published a consensus statement recommending nephrology referral of all CKD patients with a serum creatinine concentration greater than 2 mg/dL in men or greater than 1.5 mg/dL in women

- The National Kidney Foundation (NKF) also recommends early referral to the nephrology team

Components of End-Stage Renal Disease Care Preparation

- A multidisciplinary clinic approach
- Team
  = physicians,
  = social workers
  = nutritionists
  = Nurse coordinators, enhances the preparation of CKD patients for entry into ESRD care and initiation of RRT

- A multidisciplinary predialysis program
  = Reduce urgent dialysis %
  = Decreased the number of hospital days during the first month of RRT
  = Reduced costs per patient
  = Education about the various dialysis options
    - Informed choices about the appropriate modality of RRT

- Early nephrology referral allows adequate time for the dialysis care team to assist in this aspect of CKD patient care
  - = Emotionally traumatic news for most patients
  - = Discuss modality options for RRT
    - Hemodialysis
    - CAPD
    - Preemptive renal transplantation

- Patient’s preferred choice of RRT

  = PD → patient and/or the family → initiate PD training prior to the actual initiation of dialysis

= HD → vascular access → AVF at nondominant arm

→ protect their nondominant arm
(protect veins for future AVF or AVG creation)

→ Avoiding dialysis catheters

→ encourage placement of permanent vascular access
(S.creatinine > 4 mg/dL, the CrCl < 20 mL/min,or
the development of ESRD is anticipated within1yr)

= Preemptive renal transplantation

→ requires a significant amount of time for planning and completion of medical testing

- Medical management without dialysis
  = Poor candidates for chronic dialysis therapy

  = Patient may elect not to initiate RRT
    - Explicit counseling that outlines the serious consequences of this choice is mandatory
    - Should include one or more members of the patient's family

- If this decision is ultimately chosen by the patient and is supported by the family

- End-of-life care should be pursued

Components of End-Stage Renal Disease Care Preparation

- A multidisciplinary clinic approach

- Team
  = Physician
  = Social workers
  = Nutritionists
  = Nurse coordinators, enhances the preparation of CKD patients for entry into ESRD care and initiation of RRT

Kidney disease progresses to ESRD

- Dietary modifications are necessary = Avoid life-threatening
  - Volume overload
  - Hyperkalemia
  - Protein and caloric malnutrition
  - Exacerbation of metabolic acidosis
  - Divalent ion derangements

- Nephrologist = Medication adjustments
- Renal dietician
  = Essential to avoid or reduce the development
  = Nutritional state → assessed regularly
  = Dietary counseling → optimize protein intake

- To avoid information overload and patient confusion
  = Introduction of small amounts of new information at successive visits
  = Reduce patient stress
  = Improve understanding of their disease process and ultimate ESRD care plan
  = Reinforcement of correctly understood information and
  = Clarification of erroneous aspects of the patient's education
  = Early education improves understanding by reducing anxiety and fear

- Through preparation
  = Allowing for choices
  = Assuring informed consent
  = Encouraging independence
  = Promoting a sense of patient self-control

Initiation of Renal Replacement Therapy

- Timely initiation of RRT is the final aspect of adequate preparation of the CKD patient

- Absolute indications for dialysis
  = Uremic serositis (especially pericarditis),
  = Uremic encephalopathy
  = Refractory metabolic acidosis
  = Hyperkalemia
  = Uncontrollable volume overload

- Combination of the presence of signs and symptoms of uremia, kidney function as assessed by estimated GFR (or CrCl), and patient preference

- Emotional and physical preparation of patients is key

- Allows for a smooth transition and more stable entry into ESRD care or preemptive transplantation

- Early initiation of RRT for patients with advanced CKD became
  = Increasingly accepted
  = Positive results from observational studies and publication of clinical practice guidelines

- Early dialysis = Decrease mortality
  = Decrease hospitalizations
  = Decrease cost of treatment

- The Netherlands Cooperative Study on the Adequacy of Dialysis Study Group (NECOSAD)
  = 253 patients
  = started RRT at different GFR levels:
    - Timely manner (GFR 7.1 $\pm$ 2.4 mL/min/1.73 m^2)
    - late (GFR 4.9 $\pm$ 1.7 mL/min/1.73 m^2)
  = A small gain in survival time over 3 years
  in the timely start group (2.5 months)
  = No significant difference in survival between 2 groups with long-term follow-up

- This and other studies raised questions about the questionable benefit of earlier initiation of RRT

- A multicenter RCT
  = 828 adult patients with progressive CKD
  = Randomized to either early (CrCl 10 to 14 mL/min) or late (CrCl 5 to 7 mL/min)
  = No difference in mortality
  = No difference in the secondary outcomes (cardiovascular events, infectious events and complications of dialysis)

- 81,176 relatively healthy ESRD patients
  = The unadjusted 1-year mortality
    - 6.8% in those with GFR less than 5 mL/min/1.73 m2
    - 20.1% in those with GFR equal or >15 mL/min/1.73 m^2,

- Supporting the potential harm associated with early initiation of RRT

FUNCTIONS of KIDNEY

1. The kidney maintains the extracellular environment through
   = Excretion of waste products
   = Proper electrolyte and water balance

2. Several hormones are produced in the
   = Renal hemodynamics
   = Stimulate red cell production,
   = Maintain normal bone homeostasis

- Excretion of waste products
  = Urea, creatinine, uric acid, and other substances
- Balanced excretion of water and electrolytes
- Regulates systemic and renal hemodynamics
  = Production of various hormones
  = Regulation of vascular reactivity and renal blood flow/
  salt and water balance
- Hormones
  = Renin
  = Angiotensin II (AII)
  = Prostaglandins (PGs)
  = Endothelin
  = Nitric oxide
  = Adenosine
  = Bradykinin

- Produces other hormones = Influence various end-organ functions
- Renal erythropoietin synthesis
  = Red blood cell production
    = controlled by a highly regulated oxygen sensor in the proximal nephron

- Bone metabolism
  = Calcitriol
  = Proper balance of calcium and phosphorus

- Gluconeogenesis during fasting to prevent hypoglycemia

- Catabolism of various peptide hormones filtered by the glomerulus such as insulin and metabolism of peptide hormones and clearance of medications

- The most efficient hemodialysis regimens
    - 10% to 12% of the small-solute removal of two normally functioning kidneys
    - Less efficient Removal of higher-molecular-weight solutes

- Fatigue and malaise persist despite better management of anemia with erythropoietin

- Progressive cardiovascular disease (CVD), peripheral and autonomic neuropathy, bone disease, and sexual dysfunction are common, with adequate dialysis

- Patients may become dependent on family members or others for physical, emotional, and financial assistance

- Rehabilitation, particularly vocational rehabilitation, remains poor

- Kidney transplantation has the greatest potential for restoring a healthy, productive life

- Best option for treatment of CKD

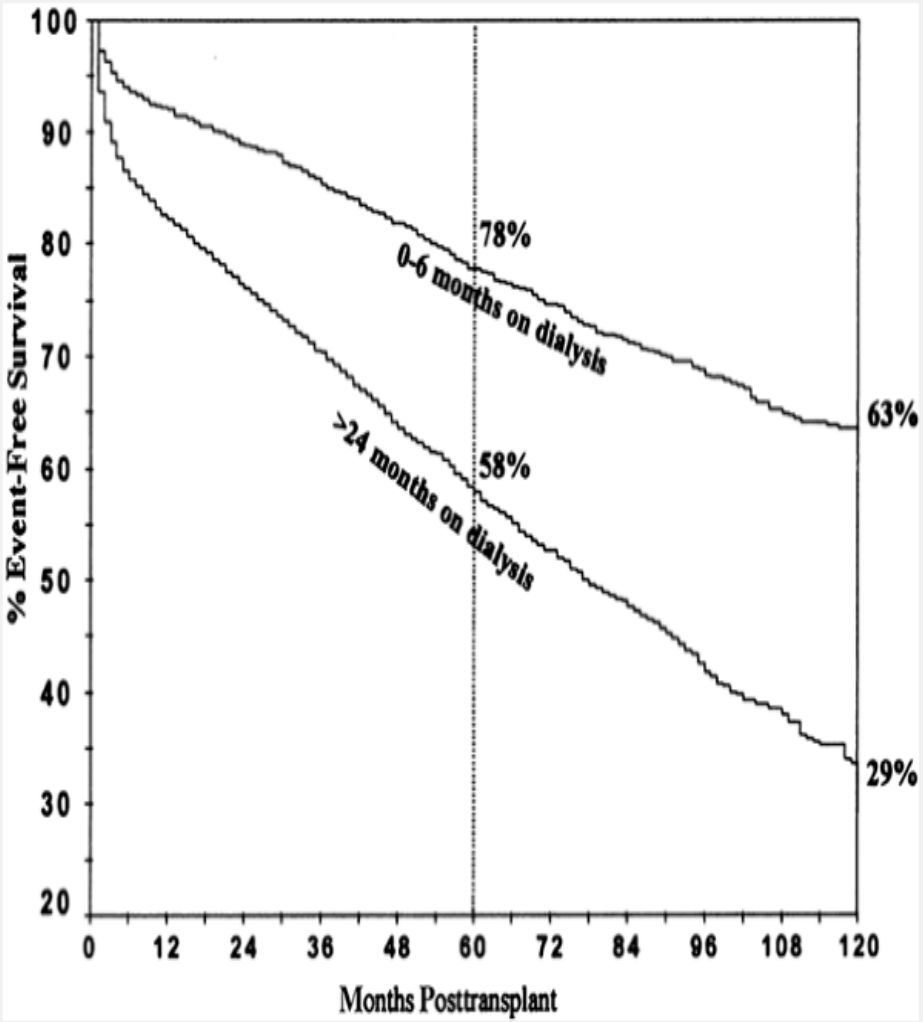


Fig. 1.4. Unadjusted graft survival in 2,405 recipients of paired kidneys with short compared to long ESRD time. (From Meier-Kriesche HU, Kaplan B. Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: a paired donor kidney analysis. *Transplantation* 2002;74:1377, with permission.)

BEST TREATMENT OPTION FOR ESRD: TRANSPLANTATION

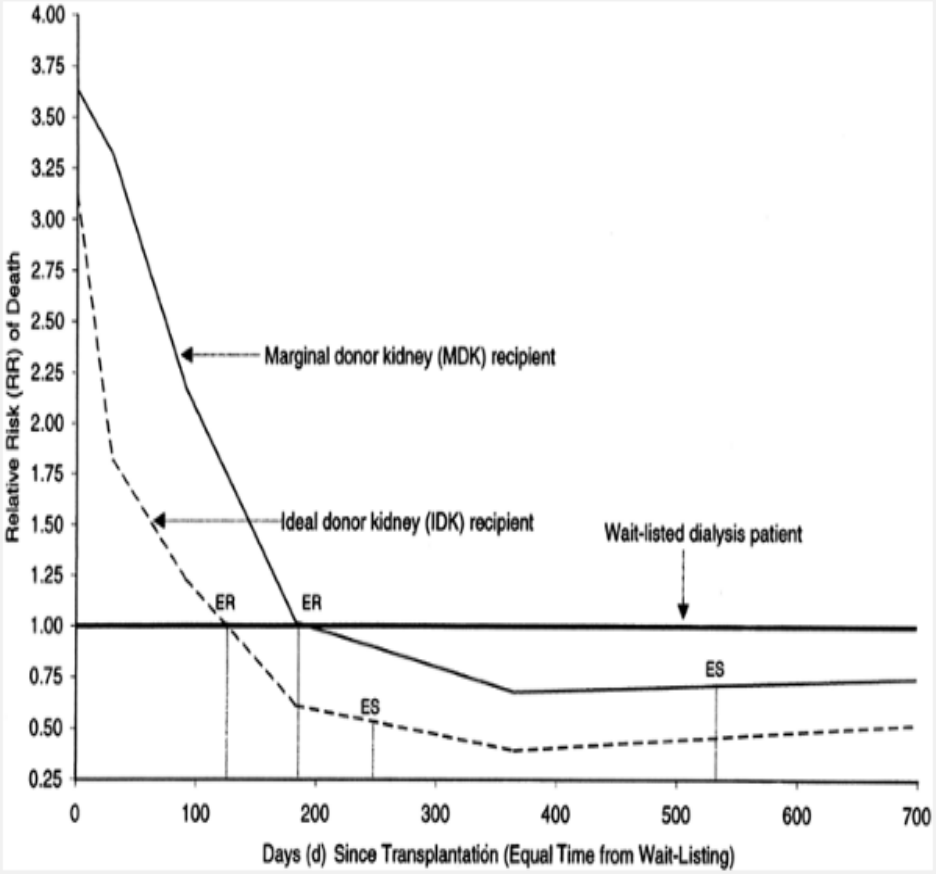


Fig. 1.5. Survival benefit of transplantation versus remaining on the waiting list for recipients of "ideal" (*interrupted line*) and "marginal" (*solid line*) kidneys (see Chapter 5). Note that in the early period after a transplant the risk of death is higher for transplant recipients than for wait-listed patients. Within a short period, somewhat longer for recipients of marginal kidneys, the risk of death (*ER*) and chances of survival (*ES*) equalize. Thereafter, transplantation has a persistent survival benefit. (From Ojo AO, Hanson JA, Meier-Kriesche H, et al. Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. *J Am Soc Nephrol* 2001;12:589, with permission.)

Evaluation and Preparation of Renal Transplant Candidates

EVALUATION OF TRANSPLANT CANDIDATES

THE TRANSPLANT REFERRAL PROCESS

The Benefits of Early Referral

- Preparation for transplantation begins as soon as progressive CKD is recognized

- Chronic renal disease care, care on dialysis, and transplant care are interdependent

- Increased cardiovascular risk - a major determinant of posttransplant morbidity and mortality

- Early referral of patients to nephrologic care during the course of CKD permits better preparation for dialysis and transplantation

- Patients who are referred to the care of a nephrologist at least 1 year before commencement of renal replacement therapy are documented to have decreased morbidity and mortality

- Preemptive transplantation - Transplantation before the commencement of dialysis
- Improve posttransplant graft and patient survival

- Five- and 10-year graft survival is 20% to 30% better (either received no dialysis or less than 6 months of dialysis than it is for those who received more than 2 years of dialysis)

- The benefit of preemptive transplantation is likely largely a result of the avoidance of the cardiovascular consequences of long-term dialysis

- The great advantage of early referral
  = Recognition and evaluation of potential living donors
  = Elective timing of the transplant
    avoid dialysis and the necessity for placement of dialysis access

- Avoidance of access placement is a great and tempting benefit
  but it must be considered carefully

- A living donor availablity = ?
- Consider a permanent access to avoid temporary access techniques
  = added morbidity

THE EVALUATION PROCESS

Patient Education

- Patient education is at the core of the process

- Transplant evaluation not only implies the medical assessment of the potential recipient by the transplant team

- The assessment by the patient of transplant option and its relevance to their well-being

- All potential transplant candidates should be encouraged to attend an information session, preferably accompanied by family members and friends

  = Risks of the operation

  = Side effects and risks of immunosuppression

  = Surgical procedure and its complications

  = The relative benefits of LDKT and DDKT
  compared and contrasted

  = Graft survival and morbidity statistics

  = The nature of rejection

  = Increased risk of infection, posttransplant tissue malignancy and mortality

- Patients should be warned - A successful transplant may not last forever
  - May return to dialysis

- The importance of compliance
  = Dialysis and dietary prescription (Pretransplant period)
  = Immunosuppressive therapy (posttransplant period)

- The possibility of posttransplant pregnancy should be discussed with women of childbearing age

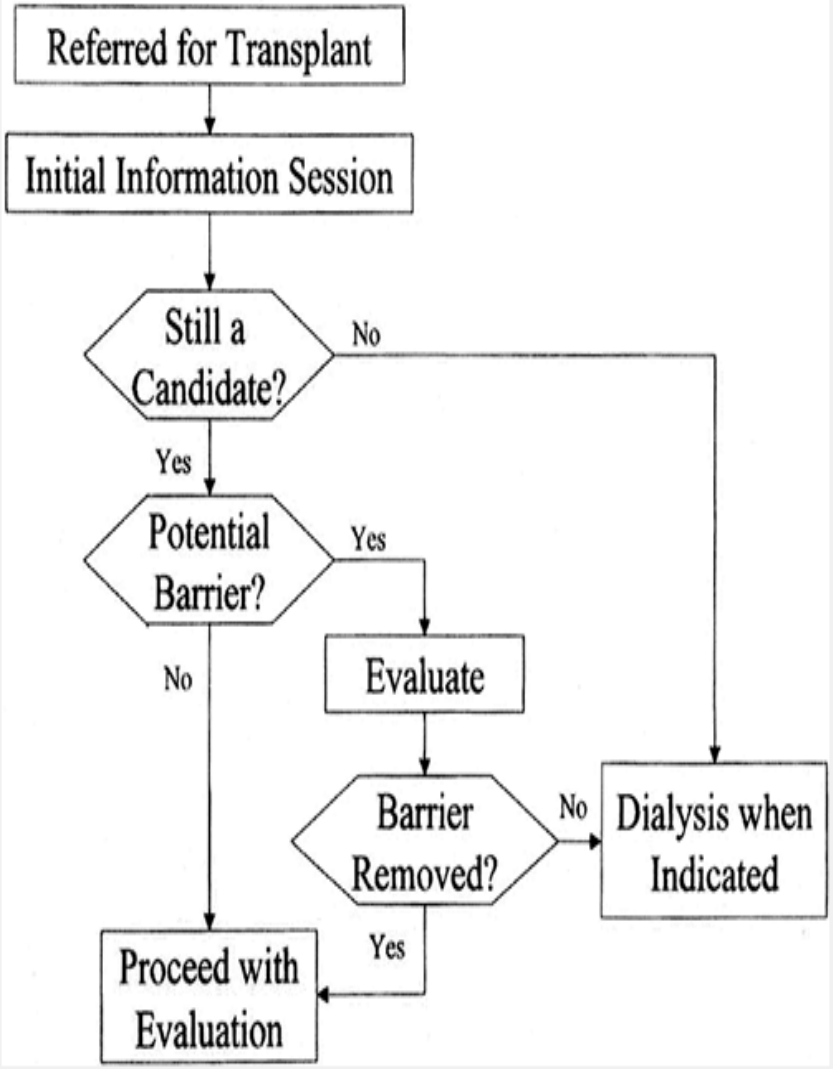


Fig. 6.1. The renal transplant candidate evaluation process. (From Kasiske BL, Cangro CB, Hariharan S, et al. The evaluation of renal transplant candidates: clinical practice guidelines. *Am J Transplant* 2001;1(Suppl 2):1–95.)

Table 6.1. Major contraindications to kidney transplantation

Recent or metastatic malignancy[a]
Untreated current infection
Severe irreversible extrarenal disease
Recalcitrant treatment nonadherence
Psychiatric illness impairing consent and adherence
Current recreational drug abuse
Recurrent native kidney disease
Limited, irreversible rehabilitative potential
Prinary oxalosis

Table 6.4. Risk of recurrent disease after renal transplantation

Focal and segmental glomerulosclerosis	30%–50%
IgA nephropathy	40%–60%
MPGN-I	30%–50%
MPGN-II	80%–100%
Membranous nephropathy	10%–30%
Diabetic nephropathy	80%–100% (by histology)
HUS/TTP	50%–75%
Oxalosis	80%–100%
Wegener disease	<20%

MPGN-II	80%–100%
Membranous nephropathy	10%–30%
Diabetic nephropathy	80%–100% (by histology)
HUS/TTP	50%–75%
Oxalosis	80%–100%
Wegener disease	<20%
Fabry disease	<5%
Systemic lupus erythematosus	3–10%

HUS, hemolytic uremic syndrome; MPGN, membranoproliferative glomerulonephritis; TTP, thrombotic thrombocytopenic purpura.

Types of Donor

I. Living Donor

II. Deceased donor organ

I. Living Donor

1. Biological Related Donor
   - a parent, sibling or child
2. Biological Unrelated Donor

(a) Emotionally related

- An apparent or easily documented close and long-standing relationship with the recipient (spouse, significant other, close friend, adopted sibling)

(b) Altruistic donor

- Absolutely no personal relationship with the potential recipient, but who have the desire to donate a kidney “to benefit mankind” or, more specifically, to improve one person's life even though they do not know the recipient.

3. Paired donor exchange

(e.g., an A to B couple “swaps” with a B to A couple)

ABO incompatiblity

4. Paid donation

KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors

(KDIGO) Living Kidney

Donor Work Group (Transplantation 2017;101(8S): S1–S109)

- GOALS OF EVALUATION, FRAMEWORK FOR DECISION-MAKING, AND ROLES AND RESPONSIBILITIES

- Goals and Principles of Evaluation

Goals and Principles of Evaluation

1.1: The donor candidate's willingness to donate a kidney voluntarily without undue pressure should be verified.

1.2: The benefits and risks of kidney donation should be assessed for each donor candidate.

1.3: The decision to accept or exclude a donor candidate should follow transplant program policies.

CHAPTER 3: COMPATIBILITY TESTING, INCOMPATIBLE TRANSPLANTATION, AND PAIRED DONATION

Evaluation

3.1: Donor ABO blood typing should be performed twice before donation to reduce the risk of unintended blood type incompatible transplantation.

3.3: Human leukocyte antigen (HLA) typing for major histocompatibility complex (MHC) Class I (A, B, C) and Class II (DP,DQ,DR) should be performed in donor candidates and their intended recipients, and donor-specific anti-HLA antibodies should be assessed in intended recipients.

Counseling

3.4: Donor candidates who are ABO blood group or HLA incompatible with their intended recipient should be informed of availability, risks, and benefits of treatment options, including kidney paired donation and incompatibility management strategies.

Table 5.3. Exclusion criteria for living kidney donors

Absolute

Cognitive deficit severe enough to cause inability to comprehend risk ofdonation

Inadequately treated psychiatric disease

Active drug or alcohol abuse

Evidence of renal disease (low GFR, albuminuria/proteinuria, unexplained hematuria and pyuria)

Significantly abnormal renal anatomy

Recurrent nephrolithiasis or bilateral kidney stones

Collagen vascular disease

Diabetes

Hypertension

Prior myocardial infarction or treated coronary artery disease

Moderate to severe pulmonary disease

Current neoplasm (unless *in situ* nonmelanoma skin cancer, cervical orcolon—excludes *in situ* bladder carcinoma)

History of cancer (lung, breast, renal or urologic, melanoma, gastrointestinal, hematologic)

Familial history of renal cell cancer

Active infection

Chronic active viral infection (hepatitis B or C, HIV, HTLV)

Significant chronic liver disease

Significant neurologic disease

History of cancer (lung, breast, renal or urologic, melanoma, gastrointestinal, hematologic)

Familial history of renal cell cancer

Active infection

Chronic active viral infection (hepatitis B or C, HIV, HTLV)

Significant chronic liver disease

Significant neurologic disease

Disorders requiring anticoagulation

Current pregnancy

History of thrombotic disease with risk factors for future events (such as anticardiolipin antibody, factor V Leiden mutation)

Relative

ABO incompatibility

Age <18 or >65 years

Obesity (especially BMI >35)

Mild or easily treated hypertension

Single prior episode of nephrolithiasis

Borderline urinary abnormalities

Younger donor with more than one first-degree relative with diabetes, or family history of renaldisease

History of gestational diabetes

Current tobacco use

Jehovah's Witness

GFR, glomerular infiltration rate; HIV, human immunodeficiency virus; HTLV, human T-lymphotropic virus.

GFR after Kidney Donation

GFR declines after kidney donation. A person with a pre-donation GFR of at least 90 mL/min per 1.73 m2 would be expected to have a 1-year post donation GFR of at least 60 mL/min per 1.73 m2

- In prior guidelines a GFR level of 80 mL/min is frequently cited as the minimal threshold for an acceptable level of kidney function for donation.

- hemodynamic alterations associated with hyperfiltration after reduction in renal mass are followed by development of structural and functional abnormalities associated with kidney disease.

- The risk of ESKD after kidney donation does not exceed ESKD risk in the general population

- An analysis of living kidney donors in the United States between 1994 and 2003 quantified a post donation ESKD rate of 0.134 per 1000 person-years over an average follow-up of 9.8 years, which was not higher than the ESKD rate in the general population, even though GFR is lower.

- Based on linking 96 217 donors from the US donor registry and healthy participants drawn from the National Health and Nutrition Examination Survey III to national ESKD reporting forms, Muzzale et al estimated that the cumulative incidence of ESKD at 15 years was 30.8 per 10 000 in donors compared with 3.9 per 10 000 in matched donors (risk attributable to donation of 26.9 per 10 000).

- In this study, the incidence of ESKD was higher in individuals who are older versus younger at the time of donation, in men versus women, in blacks versus whites, and in biologically related versus unrelated donors, but risk based on pre-donation eGFR was not reported. Based on these findings, the likelihood of a small increase in ESKD risk should be discussed with donor candidates

- Post KT MX – F/U Life long
  = I S
  = Infections (Prophylaxis, Early detection and effective treatment)
  = Regular drug monitoring
  = Renal function assessment regularly
  = Cardiovascular disease development
  = DM
  = Malignancy

Take home message

1. Late referral to the nephrology care team is associated with increased morbidity and mortality in CKD patients.
2. A multidisciplinary clinic approach (physicians, social workers, nutritionists, and nurse coordinators) enhances the preparation of CKD patients for entry into ESRD care
3. Initiation of RRT is based primarily on the presence of signs of symptoms of uremia, and the level of kidney function.
4. KT is a gold standard Tx of ESRD
5. Post KT = Survival of both patients and Graft kidney is important.
6. CKD management needs A multidisciplinary clinic approach.

A TEAM WORK

References

1. Robert F. and Mark A (2014). Nephrology in 30 Days
   Second Edition
2. Handbook of Kidney Transplantation, 4th Edition

3. UMHS Chronic Kidney Disease Guideline, March 2014

4. KDIGO 2016 CLINICAL PRACTICE GUIDELINE UPDATE ON DIAGNOSIS, EVALUATION, PREVENTION AND TREATMENT OF CKD-MBD

5. KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors, 2017

THANK YOU VERY MUCH

FOR

YOUR KIND ATTENTION