This Medical Guidance is intended to facilitate the Utilization Management process. It expresses Molina’s determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member’s benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member’s benefit plan to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS’s Coverage Database can be found on the following website: http://www.cms.hhs.gov/center/coverage.asp.

Kidney transplantation is a procedure not subject to FDA regulation.

The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this Molina medical coverage guidance (MCG) document and provide the directive for all Medicare members. The directives from this MCG document may be followed if there are no available NCD or LCD documents available and outlined below.

CMS does not have any NCD’s or LCD’s available for kidney transplantation in the adult or pediatric population.

All transplants require prior authorization from the Corporate Transplant Department. Solid organ transplant requests will be reviewed by the Corporate Senior Medical Director or qualified clinical designee. If the criteria are met using appropriate NCD and/or LCD guidelines, state regulations and/or MCG policies the Corporate Senior Medical Director’s designee can approve the requested transplant.

Members must meet UNOS guidelines for transplantation and the diagnosis must be made by a Nephrologist and or Transplant Surgeon.

Pre-Transplant Evaluation:
General requirements for transplant evaluation include all of the following:

- History and physical examination
- **Psychosocial evaluation and clearance**: This must be completed and documentation submitted for review before any additional transplant work-up or testing is initiated.
- Dietary consult
- Coronary artery disease screening:
  - One chronic smokers
  - > 50 years age
  - those with a clinical or family history of heart disease or diabetes should be evaluated with testing in the following order:
    1. thallium stress test and if these results are positive,
    2. cardiac catheterization
- Chest x-ray
- EKG
- Ultrasonography (abdomen and pelvis including kidneys, ureters, and a post-void bladder image), if abnormal additional studies may be necessary in the following order:
  1. voiding cystourethrogram
  2. cystoscopy
  3. retroperitoneography
  4. renal CT
- Bladder biopsy indicated if bladder fibrosis or cancer is suspected
- Lab studies:
  - Blood type, complete blood count, blood urea nitrogen, creatinine, electrolytes, calcium, phosphorous, albumin, liver function tests, prothrombin time, and partial thromboplastin time
  - Serologic testing for HIV, cytomegalovirus, varicella virus, herpes simplex virus, Epstein Barr virus, hepatitis virus A, B, and C, RPR, and FTA:
    - Liver function tests are indicated if hepatitis screening is positive
  - Urinalysis and urine or bladder wash culture
  - HLA Antibody

Within the last 12 months the following is required:

- Colonoscopy (if indicated or > age 50) with removal of any polyps
- Dental examination: Contact Plan for coverage criteria
- GYN examination with Pap smear (if indicated or > age 18) with complete workup and treatment of abnormal results as indicated
- Immunizations up to date when indicated: Hepatitis A and Hepatitis B, pneumococcal vaccine, influenza vaccine, tetanus booster and all childhood vaccinations
- Mammogram (if indicated or > age 40) with complete workup and treatment of abnormal results as indicated
- Osteoporosis screening with DEXA Scan:
  - One indicated for cholestatic disorders
  - prolonged corticosteroid therapy
  - postmenopausal women
Adult and Pediatric Criteria for Transplantation

Kidney transplantation from a deceased or a living donor is considered medically necessary in adult and pediatric members that have met all of the following criteria:

- Renal insufficiency with uremia or impending/current end stage renal disease (ESRD) with poor renal function documented by progressive and irreversible deterioration in renal function over the previous 6-12 months and ONE of the following:
  - Currently on dialysis; OR
  - Anticipated date of the member requiring dialysis would be within the next 6 months; AND

  - In adults or are 18 years and older: the measured or calculated glomerular filtration rate < 20 mL/min⁴⁴; OR
  - In children who are below age 18 years the measured or calculated glomerular filtration rate < 30 mL/min⁵⁴; AND

- No behavioral health disorder by history or psychosocial issues[One]:⁵⁸
  - if history of behavioral health disorder, no severe psychosis or personality disorder
  - mood/anxiety disorder must be excluded or treated
  - member has understanding of surgical risk and post procedure compliance and follow-up required to effectively manage the lifelong need for immunosuppression

Note: Patient’s need to understand the importance of adherence to medication schedules and follow-up appointments/noncompliance is a major cause of graft failure.⁵⁸

  - Adequate social/family support⁵⁸

- Documented minimal cardiovascular risks as evidenced by:
  - Negative thallium stress test and/or absent or mild coronary artery disease (noninvasive assessment)
  - Negative EKG/Echocardiogram
  - Ejection fraction above 40% and pre-operative cardiac evaluation
  - Absence of myocardial infarction/Positive stress test within the last 6 months
Note: Clearance by a cardiovascular specialist is required prior to surgery if the above complications are present

- Serum transaminases and total bilirubin normal<sup>58</sup>
- Hepatitis serologies negative<sup>58</sup>
- No genitourinary disease by history and physical<sup>58</sup>
  - Test results negative
  - Treated/minor abnormalities

- HIV patients should be carefully evaluated and transplantation should be performed in a center that has extensive experience in HIV management and transplantation; the minimal required inclusion criteria is as follows[ALL]:
  - CD4 count >200 cells/mm-3 for >6 months
  - HIV-1 RNA undetectable
  - On stable anti-retroviral therapy >3 months
  - No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioses mycosis, resistant fungal infections, Kaposi’s sarcoma, or other neoplasm)
  - Meeting all other criteria for transplantation

- Active untreated substance abuse issues, requires documentation supporting free from addiction for minimally 6 months if previous addiction was present

- The requesting transplant recipient should not have any of the following absolute contraindications:
  - Unable or unwilling to take the required immunosuppressant medications at the prescribed frequency that would result in graft failure
  - Ongoing or recurring infections (bacterial, fungal, or viral) that are high risk of reactivating with immune suppression or poorly controlled HIV
  - Malignant neoplasm with a high risk for reoccurrence, non-curable malignancy (excluding localized skin cancer)
  - Chronic illness with one year or less life expectancy

- The requesting transplant recipient should be evaluated carefully and potentially treated if the following relative contraindications are present:
  - Irreversible lung disease patients require consultation and clearance by a Pulmonologist prior to consideration of transplantation, this includes the following:
  - Severe or moderate chronic obstructive pulmonary disease (COPD), restrictive disease or pulmonary fibrosis with any of the following:
- SAO2 <90% or PO2 <60 mmHg with exercise desaturation
- FEV1 <25% predicted value
- > 4 lower respiratory infections within past year in severe COPD patients
- Pulmonary hypoplasia, bronchopulmonary dysplasia or other significant chronic lung disease in children require consultation with a Pediatric Pulmonologist
- Uncontrolled asthma, severe cor pulmonale, or home oxygen therapy requirement
  - Smoking (impairs microvascular and wound healing), documentation supporting free from smoking for 6 months
  - Active peptic ulcer disease
  - Active gastroesophageal reflux disease
  - CVA with long term impairment that is not amendable to rehabilitation or a patient with CVA/transient ischemic attack within past 6 months
  - Obesity with body mass index of >30 kg/m² may increase surgical risk and must be screened for cardiovascular risk.
  - Chronic liver disease such as Hepatitis B/C/D, or cirrhosis which increases the risk of death from sepsis and hepatic failure requires consultation by a gastroenterologist or hematologist
  - ESRD caused by congenital malformations (e.g., spina bifida, prune belly, vesico-ureteric reflux, bladder extrophy, posterior urethral valve, vertebral/vascular anomalies, anal atresia, tracheoesophageal fistula, esophageal atresia, renal anomalies/radical dysplasia), acquired malformations (neurogenic, tuberculosis, repeated surgery for vesico-ureteric reflux) or functional disorders of the lower urinary tract; these abnormalities require clearance by Pediatric Urologist with potential surgical correction prior to transplantation.
  - Absent bladder or sphincter insufficiency (e.g., iatrogenic, neurogenic); clearance by a Urologist is required with potential supravesical urinary diversion being performed at least 10-12 weeks prior to consideration of transplantation.
  - Gall bladder disease with symptomatic cholelithiasis requires ultrasound of the gall bladder with treatment prior to transplantation

**Note:** In the event of a request for any of the above relative contraindications, the PCP/requesting physician must provide written documentation outlining knowledge regarding the existence of the contraindication, provide a written explanation of the advantages of surgery, and explain how the advantages outweigh the risks.

**Simultaneous Liver-Kidney Transplantation:** Molina Healthcare considers a simultaneous liver and kidney transplant medically necessary when any of the following criteria are met:
- End stage renal disease (ESRD) with cirrhosis and symptomatic portal hypertension or hepatic vein wedge pressure gradient ≥10 mmHg
- Hepatic failure and GFR ≤30 mL/min due to chronic kidney disease
- Acute kidney injury (AKI) or hepatorenal syndrome with serum creatinine ≥2 mg/dL (177 µmol/L) and dialysis ≥8 weeks
- Hepatic failure and chronic kidney disease with a kidney biopsy showing >30 percent glomerulosclerosis or >30 percent fibrosis
CONTINUATION OF THERAPY

When extension of a previously approved transplant authorization is requested, review using updated clinical information is appropriate.

- If Molina Healthcare has authorized prior requests for transplantation, the following information is required for medical review: [ALL]
  - Presence of no absolute contraindication as listed above;
  - History and physical within the last 6 months;
  - Kidney profile within the last 6 months;
  - Stress test within the last 2 years (≥ 50 years of age);
  - Psychosocial evaluation or update within the last 12 months;
  - Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.

- If authorized prior requests for transplantation were obtained from another insurer, the following information is required for medical review: [ALL]
  - Authorization letter/documentation from previous insurer;
  - Presence of no absolute contraindication as listed above;
  - History and physical within the last 6 months;
  - Kidney profile within the last 6 months;
  - Stress test within the last 2 years (≥ 50 years of age);
  - Psychosocial evaluation or update within the last 12 months;
  - Per initial and updated history and physical, any other clinically indicated tests and/or scans as determined by transplant center physician or Molina Medical Director.

COVERAGE EXCLUSIONS

Kidney transplantation from a deceased or a living donor is considered not medically necessary under the following circumstances:

1. If any evidence of the following absolute contraindications exist:
   - Severe uncorrectable or high risk cardiac disease with an ejection fraction below 40% and/or positive myocardial infarction/positive stress test within the past six months
   - Unable or unwilling to take the required immunosuppressant medications at the prescribed frequency that would result in graft failure
   - Active untreated substance abuse issues, or smoking (impairs microvascular and wound healing), or documentation supporting free from addiction or smoking for minimally 6 months
   - Ongoing or recurring infections that are high risk of reactivating with immune suppression bacterial, fungal or viral (screening for tuberculosis, CMV, Epstein Barr, and treatment if positive)
   - AIDS (CD4 count < 200cells/mm3)
   - If HIV positive all of the following are met to remove as a contraindication:
     - CD4 count >200 cells/mm-3 for >6 months
     - HIV-1 RNA undetectable
     - On stable anti-retroviral therapy >3 months
No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioses mycosis, resistant fungal infections, Kaposi’s sarcoma, or other neoplasm)

Meeting all other criteria for transplantation

- Malignant neoplasm with a high risk for reoccurrence, non-curable malignancy (excluding localized skin cancer) or metastatic cancer; recommended waiting period post cancer treatment is minimally 2 years for most cancers
- Chronic illness with one year or less life expectancy

2. The requesting transplant recipient should be evaluated carefully and potentially treated if the relative contraindications are present as outlined in ‘Coverage Criteria’ section noted above; specialist clearance for surgery as appropriate is required.

3. Requests for third or subsequent kidney transplantation require medical necessity review.

**DESCRIPTION OF PROCEDURE/SERVICE/PHARMACEUTICAL**

Kidney transplantation is a surgical procedure performed to remove a healthy functioning kidney from a living or brain-dead donor and surgically attaching it into an individual diagnosed with irreversible end stage renal disease or chronic renal failure. End stage renal disease occurs when kidneys are damaged from a disorder, disease or a congenital condition. The kidneys’ ability to function properly is impaired. The kidneys ability to properly remove and filter fluid and waste from the body and regulate specific chemicals in the bloodstream is impaired. Non-functioning kidneys may or may not be removed during the procedure. Generally, the nonfunctioning kidneys are left in place and the transplanted kidney is surgically attached in a different location near the nonfunctioning kidney(s); this process decreases the potential for surgical morbidity. The existing nonfunctioning kidneys are removed if persistent infection, hypertension or interference with the new organ is experienced.

**GENERAL INFORMATION**

Summary of Medical Evidence

Prevalence

Kidney transplantation is the most common solid organ transplantation performed and is indicated in end-stage renal failure. It is the second most common transplant following corneal transplantation in the United States. According to the Organ Procurement and Transplantation Network (OPTN) 16,814 kidney transplants were performed in 2011. According to Himmelfarb (2007), “In the United States, more than 400,000 individuals have end-stage renal disease (ESRD), for which life can be sustained only with renal replacement therapy such as dialysis or kidney transplantation. In a recent population-based study of US residents 45 years and older, 9.5% had a first degree relative with ESRD. It is estimated that by 2015, more than 700,000 individuals in the United States will have ESRD, and more than 107,000 ESRD related deaths will occur annually.”
The incidence and prevalence of kidney failure treated by either dialysis or transplantation has increased from 1988 to 2004 in the United States. A cross sectional analysis of adults aged 20 and older during 1988-1994 (n=15,488) and 1999-2004 (n=13,233) was performed using the National Health and Nutrition Examination Surveys. Albuminuria persistence (>30mg/g) and glomerular filtration rate increases (GFR) were the outcome measures used. The prevalence of both measures showed an increase in chronic kidney disease (CKD) from 1999-2004. The authors indicated that the increased prevalence of diagnosed hypertension and diabetes with larger body mass are strong factors contributing to the results. The study results showed CKD stages 1 to 4 increased from 10% to 13.1% overall with 95% confidence interval in all categories; Stage one increased from 1.7 to 1.8%, Stage two- 2.7 to 3.2%, Stage three- 5.4 to 7.7%, and 0.21% to 0.35% for Stage four. The prevalence of both measures showed an increase in chronic kidney disease (CKD) from 1999-2004. The authors indicated that the increased prevalence of diagnosed hypertension and diabetes with larger body mass are strong factors contributing to the results. The study results showed CKD stages 1 to 4 increased from 10% to 13.1% overall with 95% confidence interval in all categories; Stage one increased from 1.7 to 1.8%, Stage two- 2.7 to 3.2%, Stage three- 5.4 to 7.7%, and 0.21% to 0.35% for Stage four. The high risk populations associated with the development of kidney disease include individual’s with:

- A diagnosis of hypertension with and without cardiovascular disease
- Diabetes
- Bladder Obstruction
- A family history of kidney disease
- First Nations and Pacific Islanders high risk ethic groups and ethnic minority populations
- 60 years of age and older

Research Study Evidence

The majority of evidence based research conducted for kidney disease and transplantation procedures are from epidemiologic studies derived from databases and registries such as the United States Renal Data System registry and the Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients (OPTN/SRTR) annual report. Population surveys and longitudinal cohort studies have also been conducted to provide additional information and investigation on kidney disease and treatment. There is paucity of randomized clinical trials relating to nephrology. The Cochrane Renal Group has reported that only approximately 1.15% of all citations in the literature from 1966 to 2002 are randomized clinical trials in nephrology making this area the third lowest of 13 medical specialties reviewed.

Patient and Graft Survival Rates

According to the 2006 Organ Procurement and Transplantation Network/Scientific Registry of Transplant Patients (OPTN/SRTR) annual report, living donor survival and graft survival rates are better than deceased donor rates after 1, 3, 5 and 10 years. Graft survival after 1 year in living donors was 95.1% versus 89.5% in deceased donor kidneys, 3 years the graft survival in living donors was 88.4% versus 78.6% 5 years 80.3% versus 67.1% and after 10 years graft survival in living donor’s decreases to 56.5% versus 40.8%. Patient survival was 98% in living donors following 1 year versus 94.7%, 3 years 94.5% versus 88.1%, 5 years 90.4% versus 80.7% and after 10 years 76.4% compared to 60.7%.
The OPTN/SRTR report also identifies glomerular disease as the top diagnosis requiring transplant in recipients from 1996 to 2005. Diabetes, hypertensive nephrosclerosis, polycystic kidneys, tubular and interstitial disease and congenital and familial related diseases were the next most common diagnoses listed in descending order according to volume. Patient and graft survival rates are consistently less successful when compared to all other age groups in recipients 65 and older. Patient survival after 3 years in the age 65 and older group is 86.9% and 75.4% after 5 years in living donors, and 79.5% and 63.9% respectively in deceased donor recipients. Graft survival after 3 years is 74.5% and 59.7% after 5 years in the 65 year and older group. Children of all ages have shown patient and graft survival rates similar to adults. A study conducted in New Zealand and Australia indicated the risk for death in children receiving dialysis is four times greater than with renal transplantation. Although survival rates in the 65 year old or greater group, are lower in comparison to other age groups, literature indicates recipient age is no longer considered a contraindication to transplantation as evidenced by acceptable patient and graft survival rates.

Kidney transplantation performed in 321 children 13 years or younger found no significant differences in patient or graft survival rates in ages 1 year or less, 1 to 4 years, and 5 to 15 years. Almost all our infant (<1 year) recipients received organs from living donors (LDs); a comparison of living donors among the three groups were also without significant differences. All infant recipients in 2004 from the date of the written report were alive and well, 24 (80%) with a functioning original graft. According to Macdonald et al. (2004) “causes of the 6 graft losses were chronic rejection (n=3), vascular thrombosis (n=2), and recurrent disease (n=1). Infants had significantly lower incidences of acute and chronic rejection compared with older recipients, but a tendency to higher incidences of delayed graft function and vascular thrombosis. Infants had significant increases in weight post transplant: the mean standard deviation score rose from -2.8 pre-transplant to -0.2 by age 5 years and to +1.8 by age 10 years. The improvement in height was less marked: the mean standard deviation rose from -3.2 pre-transplant to -1.6 by age 5 years and to -1.4 by age 10 years. Kidney transplant results in very young children can be comparable to those in older children.”

Complications

Kidney transplantation is associated with several potential complications, of which the most significant is rejection of the transplanted kidney or graft. The required use of ongoing immunosuppressant medications contribute to post surgical complications such as infection, diabetes mellitus, high cholesterol, cancer, gastrointestinal toxicity, and bone disease. Some form of kidney disease may also reoccur in the transplanted kidney. Cardiovascular risk factors are also seen in both children and adults post transplantation and are one of the major causes of death post transplantation in approximately 42% of transplanted kidneys. Some studies have also associated anemia or neutropenia as a significant factor associated with graft failure and mortality post transplantation.

Cardiovascular complications have consistently been reported as one of the leading causes of death in renal transplantation recipients. Proper management of cardiac disease requires evaluation and treatment of preexisting disease in high risk patients. In studies evaluating mortality with graft function within 30 days post transplantation cardiovascular disease attributed to approximately 47.1%. It is generally recommended
to evaluate cardiovascular status through a medical history in individuals at high risk for cardiovascular disease. Patients with a history of heart disease should undergo cardiac stress testing and possible angiography if the stress test is positive prior to consideration for transplantation.\textsuperscript{30} Absolute contraindications to transplant would include myocardial infarction within the past 6 months, ejection fraction below 40-50\% with uncorrectable coronary artery disease.\textsuperscript{23}

Infection should be treated prior to transplantation. The presence of a persistent infection may become life threatening post transplantation especially with the use of immunosuppressant medications. Screening for tuberculosis, Cytomegalovirus, varicella virus, herpes simplex virus, tuberculosis, Epstein Barr virus, RPR, and FTA, hepatitis, A,B,C should be conducted and treated prior to transplantation.\textsuperscript{16,30}

Cerebral vascular disease (CVA) is more prevalent post transplantation. According to studies, the cumulative incidence of cerebral vascular disease increases to 15\% after 15 years.\textsuperscript{35} Stroke following transplantation have reported mortality rates at 50\% post transplantation.\textsuperscript{45} High risk individuals for post transplant CVA include diabetes, hypertension, cigarette smoking, hyperlipidemia, and age. According to Knoll et al, “Kidney transplantation should be deferred in patients with a history of stroke or transient ischemic attack for at least 6 months following the event. The patient should be stable and fully evaluated and treated with risk-reduction strategies before kidney transplantation.”\textsuperscript{44} Another study indicated peripheral vascular disease (PVD) was 3\% more prevalent post transplantation after a 4 year evaluation of 406 stable transplant recipients.\textsuperscript{36} A retrospective study of 664 adult kidney transplant recipients indicated a 4.2\% cumulative incidence of PVD associated with claudication, amputation or revascularization after 5 years and 5.9\% after 10 years.\textsuperscript{37} CVA and PVD are considered relative contraindications that carry greater risk of posttransplantation complications.\textsuperscript{23} These risks must be considered and discussed with patients before transplantation occurs.\textsuperscript{30}

Cancer has been reported to be responsible for 9-12\% of renal transplant recipient deaths. Information contained in the Cincinnati Transplant Tumor Registry (CTTR) indicates “54\% of cancer recurrences occurred in patients who had their pretransplant malignancies treated within 2 years of transplantation, 33\% of recurrences occurred in patients treated 2-5 years before transplantation and 13\% of recurrences occurred in patients treated more than 5 years before transplantation”.\textsuperscript{30,31,32} Literature suggests that effective screening and treatment of cancer may reduce the risk of post-transplant cancer malignancy.\textsuperscript{30}

According to Bhagnai and Sweny (2006), the use of HAART (Highly Active Antiretroviral Therapy), has been a significant factor in the successful prognosis of patients with HIV disease. As a result, an HIV patient may be considered for transplantation if CD>200cells/ul for at least 6 months, undetectable HIV viraemia (>50 copies/ml) for at least 6 months, demonstratable adherence and a stable HAART regimen for 6 months, absence of AIDS defining illness following successful reconstitution after HAART, antiretroviral treatment options are available in the future (must be discussed and confirmed by the treating HIV MD).”\textsuperscript{27}
Troppman et al. (1995) conducted an evaluation of gastrointestinal related complications. Pelvic ulcer disease (PUD) disease showed a three times greater incidence of posttransplant ulceration than patients without a history of PUD. Ulcer related mortality and graft loss were not found. It was concluded that renal transplantation can be safely performed in members with a treated history of PUD.\textsuperscript{30,33} A gastrointestinal endoscopy is generally recommended for patients with a history of PUD and treatment is recommended before consideration of transplantation.\textsuperscript{30}

Viral hepatitis has been reported as one of the previously common causes of chronic, post transplant liver disease. Mortality from liver failure has been reported between 8 to 28\% in long term kidney recipients. Hepatitis B and C have been found to be the most common hepatotropic virus infections that can have a significant impact in a renal transplant recipient. There is no evidence to suggest that hepatitis A, E or G will cause liver disease in renal transplant recipients. Hepatitis D has been associated with progression of significant liver disease but is extremely rare. It is recommended to evaluate for hepatitis prior to transplantation. Patients with liver cirrhosis have a much higher risk of liver failure post transplantation and may not be acceptable candidates for renal transplantation alone.\textsuperscript{30}

Sehgal et al. (1997) identified a high incidence of unrecognized mental impairment in hemodialysis patients, however, it remains controversial if dialyzed end stage renal patients experience marked neuro-cognitive deficits.\textsuperscript{30,38} According to Kasiske et al. (2001), “the potential recipient should have sufficient cognitive ability to weigh the risks and benefits of the surgical procedure and understand the need for life-long immunosuppression. Individuals who demonstrate difficulty with attention, assimilation or memory should be referred for a formal neuropsychiatric assessment of cognitive function. Reversible medical causes of cognitive impairment should be screened by checking thyroid function tests, thiamin, vitamin B\textsubscript{12} as well as baseline measurements of anemia, acidosis, uremia and hepatic function.”\textsuperscript{30}

The ability to adhere to required treatment protocols post transplantation may be hindered by alcohol or drug abuse.\textsuperscript{30} One study identified 25\% of patients that were evaluated prior to transplantation were alcohol or drug abusers.\textsuperscript{39} According to Kasiske et al. (2001), “Every effort should be made to ensure chemical dependency is adequately treated prior to transplantation. It is reasonable to insist that renal transplant candidates with a history of chemical dependency undergo counseling and treatment, and that caregivers document a drug-or alcohol free period of at least 6 months”.\textsuperscript{30}

Smoking has been found to contribute 5.5 times more to pulmonary complications post operatively than nonsmokers.\textsuperscript{43} According to Kasiske et al. “Patients who smoke should be offered a smoking cessation program and or pharmacological aids to smoking cessation (nicotine patches, nicotine gum etc.) and should be strongly encouraged to stop smoking before transplantation.”\textsuperscript{30}
Obesity is considered a relative contraindication to surgery. Obesity has been found to correlate with additional hospital cost and length of stay. Several sources have identified that obesity (BMI \( \geq 30 \text{ kg/m}^2 \)) has proven to have higher rates of surgical post operative complications such as infection and higher rates of delayed graft functioning, and diabetes mellitus. In one study, obese patients had a higher prevalence of hypertension (P = .028), left ventricular hypertrophy (P = .014), dyslipidemia (P = .001) and acute tubular necrosis (ATN) (P = .006), without a higher incidence of acute rejection episodes (P = .756). Postransplant diabetes mellitus was more frequent (P = .000), and systolic blood pressure (P < .05), total cholesterol (P < .05), and triglycerides were higher (P < .05). Serum creatinine at 6 months (P = .007) and proteinuria >0.5 g/24 hours, (P = .023) were also higher. Graft survival was not different between groups, but patient survival was lower in the obese group (P = .002). A logistic regression analysis showed that the recipient age (RR: 5.243) and the presence of obesity (RR: 1.100) were independent prognostic factors for patient death. In another study, 71% percent of obese patients experienced complications compared with 24.3% (P = .025) of non-obese patients. Surgical treatment was required in 29% of patients. Transplantation candidates with a BMI of >30 kg/m\(^2\) should be in a supervised weight loss program that includes increased physical activity, low calorie diet, and behavioral management program prior to transplantation with a goal weight of BMI <30kg/ m\(^2\).

Long-term survival and short term operative risks are higher in patients with irreversible lung disease. According to Knoll et al (2005), “Patients in the critical contraindication category have mortality rates that are quite high; a best FEV\(^1\) of <40% of the predicted value is associated with a 50% survival rate at 6 years follow-up”. FEV\(^1\) of less than 25% would have an even lower anticipated survival rate. Home oxygen therapy members have been documented with a 5 year survival rate of approximately 30%.

Bladder dysfunction has been associated with increased risk for the development of urinary tract infections and may impact graft outcomes. Patients with small non-compliant bladders also have an increased risk. Urinary conduit with augmentation cystoplasty may be required prior to transplantation to improve post transplantation outcomes.

**Expanded-Criteria Donor Kidneys (ECD)**

A single center, retrospective cohort study was conducted from 1999 to 2001 to evaluate the clinical and financial implications for using ECD kidneys (n=45) versus non-ECD kidneys (n=157) for transplantation in adults. Non-ECD kidneys are the gold standard as there is lower risk of graft failure. According to the authors “there was no significant difference overall between the two groups in terms of death and graft loss. The exception was for the year 2000, when there was significantly more death and graft loss among ECD patients (p=0.03). There was no statistical difference in these end points for the other years, or for the cohort overall. There were 2 cases of urethral strictures in the ECD group and none in the non-ECD (p=0.049). There was no significant difference between the two groups for other surgical complications. There was no statistically significant difference between the patients groups in patient survival, graft survival and death-censored graft survival, although these were all found to be slightly lower in the ECD cohort. The unadjusted relative risk of death censored graft failure in the ECD group was 1.58 (p=0.45). Both cohorts had similar creatinine concentrations at 1 month. However, at all other time points, until 36 months, those with functioning ECD
kidneys had statistically significant higher creatinine concentrations. The authors concluded that although there was a difference in graft survival, patient survival and death-censored graft survival between the two cohorts it was not statistically significant. They concluded that ECD kidneys should be used in transplants when the only alternative is dialysis.\textsuperscript{12}

Sellars et al. (2004) also performed a cost-consequence analysis for ECD versus non-ECD recipients. Only direct costs were included in the analysis. These costs included inpatient charges for up to one year following transplantation. A sub-group analysis evaluating each fiscal year was performed. Costs associated with organ donation acquisition were excluded as they were considered the same for both groups. No discounting was included. The authors indicated “the mean costs (+/- standard error) were $76,962 (+/- 8,288) for the ECD transplants and $71,026 (+/-4,470) for the non-ECD transplants, (p=0.531). The mean costs (+/- standard error) for patients undergoing retransplantation were $136,596 (+/-41,539) in the ECD cohort and $91,296 (+/-15,619) in the non-ECD cohort, (p=0.25)”.\textsuperscript{12} The authors concluded “expanded-criteria donor (ECD) transplants were more expensive and resulted in worse outcomes than non-ECD transplants. However, the patients were better off with ECD transplants than with continued dialysis.”\textsuperscript{12}

Kidney Transplantation versus Hemodialysis

A study performed by Wolfe et al. (1999) providing the most convincing evidence of the survival benefits by comparing mortality from patients on waiting lists for transplant and transplant recipients. This longitudinal study was conducted from 1991 to 1997 and evaluated mortality in 228,552 diagnosed with end stage renal disease that received long term dialysis. Out of these patients, 46,164 were on a transplantation waiting list of which 23,275 received a first cadaveric transplant. The study results indicated “the standardized mortality ratio for the patients on dialysis who were awaiting transplantation (annual death rate, 6.3 per 100 patient-years) was 38 to 58 percent lower than that for all patients on dialysis (annual death rate, 16.1 per 100 patient-years). The relative risk of death during the first 2 weeks after transplantation was 2.8 times as high as that for patients on dialysis who had equal lengths of follow-up since placement on the waiting list, but at 18 months the risk was much lower (relative risk, 0.32;95 percent confidence interval, .30 to 0.35; P<0.001). The likelihood of survival became equal in the two groups within 5 to 673 days after transplantation in all subgroups of patients examined. The long-term mortality rate was 48 to 82 percent lower among transplant recipients (annual death rate, 3.8 per 100 patient-years) than patients on the waiting list, with relatively larger benefits among patients who were 20 to 39 years old, white patients, and younger patients with diabetes.\textsuperscript{17}

A retrospective cohort study and cost-effective analysis was conducted between 1994 and 1997 of ESRD patients receiving transplantation versus hemodialysis treatment that were candidates for transplantation. There were 242 transplant patients and 840 control group waiting list dialysis patients. During the study 410 of the control group patients received transplantation and were removed from the control group and entered into the transplant group. A three year follow-up evaluating mortality, retransplants and graft loss were among the studied outcomes. The results indicated “the number of transplant patients who dies after 3 years’ follow-up was 40. (16.5%). The number of transplant patients who suffered graft loss was 44 (18.2%). Seven of them received successful retransplants during the study period. Patients continued on dialysis had 3.5 times greater
risk of dying after 3 years’ follow-up than did transplant patients (p<0.0001). Compared with control patients, the absolute reduction in mortality rates for transplant patients was 5.6% and the relative reduction was 27.7%.”

The clinical conclusion indicated that transplant patients have a greater probability of survival 3 years after transplantation versus those receiving dialysis after three years. The author also provided cost analysis which indicated “the 3-year costs per patients were $109, 197 (SD=47,548) for dialysis and $70, 297 (SD-29,860) for CKT. The costs of adverse complications were included in the analysis. 13

JAMA (1999) reported a study performed at the University of Maryland School of Medicine between 1996 and 1998. Living donor kidney recipients (227) transplantation costs in the first year following surgery averaged $89,939. Following the first year, the average monthly cost decreased to $16,043 which included mostly antirejection medications. It was reported average annual dialysis costs were approximately $44,000. It was reported that for the average patient after 2.7 years the patient would recoup the cost associated with the transplantation when compared with dialysis. In patients that did not require readmission, it was estimated at approximately 1.7 years. 13

Retransplantation

The survival benefit associated with kidney retransplantation has not been well studied. A study was performed using the Canadian Organ Replacement Register (CORR) with 3,067 patients initiating renal replacement therapy during 1981-1998 who had received a transplant and experienced graft failure (GF). Such patients were followed until death, loss to follow-up or the end of the observation period (December 31, 1998). Overall, retransplantation is associated with a covariate-adjusted 50% reduction in mortality, relative to remaining on dialysis (HR=0.50; P<0.0001). This benefit is most pronounced in the 18- to 59-year age group. Retransplanted patients were at significantly higher risk of death relative to patients on dialysis only during the first month of posttransplant (HR=1.66; P=0.047), and experienced significantly reduced mortality thereafter. 48

Survival benefits have been reported in a large series of more than 19,000 renal transplant recipients with primary allograft failure. A 45 percent reduction in mortality at five years in patients with type 1 diabetes and 23 percent reduction in mortality in patients without diabetes compared with waiting list patients. Failed primary transplant patients have been noted to comprise approximately 30% of the current waiting list. 49,50

Barba and colleagues (2011) conducted a retrospective study to evaluate the influence of retransplantation in graft and recipient survival. 419 renal transplants were studied regarding the influence of retransplantation in graft and patient survival. A homogeneity study was performed between the two groups with a Student’s T and a chi-square tests. Graft survival analysis was performed with Kaplan-Meyer and log rank tests. Of 419 transplants, 370 (88.3%) were first transplantations, 45 (10.7%) second transplantations and 4(1%) third ones. Mean follow-up of the whole group was 72.5 months (±54.1 SD). There were no differences in follow-up between groups (Mean Follow-up 73.1 months ±54.4 SD in first transplantations vs. 61.6 months ±51.2 SD in repeat transplantation. p >0.05). The actuarial graft survival showed no differences between patients with first transplantation and those with a repeat one. [3 and 5 year SV of 89% (95% CI: 87-91%) and 84%(95% CI: 82-
86%) Vs 88% (95% CI; 83-93%) and 85% (95% CI;i; 80-90%) respectively]. After adjusting for all the heterogeneity variables we still did not find differences on graft survival. The actuarial recipient survival showed no differences between patients with first transplantation and those with a repeat one. [3 and 5 year SV of 98% and 96% Vs.97%]. The authors concluded that there are no differences of graft and recipient survival between patients with a first transplantation and those with a repeat one. 60

Ahmed and Colleagues (2008) performed a retrospective analysis to assess the outcome of kidney retransplantation in patients receiving more than one allograft. During the 12-year period (1993-2005), 196 patients received more than one renal transplant. Of these, 163 had two (group I) and 33 had more than two transplants (group II). In group II, 24 patients had three, eight had four, and one had five consecutive allografts. The control group comprised of 100 randomly selected patients receiving a first graft during the same period. In group I, 53 (32.5%) grafts failed. Eighteen (11.0%) patients died with functioning grafts. In group II, 14 (41.2%) grafts failed while four patients (11.8%) died with functioning grafts. In group I, actuarial graft survival rates at 1, 2, 3, and 4 years were 82.3%, 67.3%, 55.97%, and 42.14%, respectively. In group II, the respective figures were 84.85%, 66.67%, 60.61%, and 51.52%. The difference was not statistically significant (P = .96). In the control group, 1-, 2-, 3-, and 4-year survival rates were 92%, 84, 74%, and 60%, respectively. The difference between the control and study groups was statistically significant (P = .0002). The authors concluded that graft survival after retransplantation is relatively inferior when compared to the primary graft but still remains fairly high. Therefore, previous graft failure should not be considered as a relative contraindication for retransplantation. 62

Hayes, Cochrane, UpToDate, MD Consult etc.

Hayes:

There is not a Directory report available for this topic. A Directory Report was available on this topic with an original copyright date of 1996. The report has been archived since 2002. A new report was not updated and reissued as it is considered standard of care. Once a technology is considered standard of care, Hayes elects to remove the report from the Directory rather than providing an update. The Hayes rating contained within the archived document in 2002 was the highest available rating for kidney transplantation for correcting uremia caused by end stage renal disease. 7

UpToDate:

Renal transplantation is the treatment of choice for children with end-stage kidney disease (ESKD) because of its greater survival rate compared with chronic dialysis and associated with better growth and developmental outcomes. A transplant evaluation is indicated when the measured or calculated glomerular filtration rate < 30 mL/min and the child is in stage 4 chronic kidney disease. Graft survival is superior with a living donor versus a deceased donor allograft. The most common cause of ESKD in children who undergo renal transplantation is congenital deformities of the kidney and urinary tract, followed by glomerular disorders, hereditary/genetic renal diseases, and focal glomerulosclerosis particularly in African American patients. Contraindications for renal transplantation include sepsis, uncontrolled extra-renal malignancies, irreversible multi-organ failure, severe cardiac and pulmonary dysfunction not corrected by organ transplant, underlying life-threatening
disorder not corrected by renal transplant, elevated levels of antiglomerular basement membrane antibodies, and a recent history of nonadherence to medical care.  

Renal transplantation is the treatment of choice for end-stage renal disease in adults. A transplant evaluation is indicated when the measured or calculated glomerular filtration rate < 20 mL/min and there is evidence of progression of irreversible kidney disease over the last 6-12 months. A successful kidney transplant improves the quality of life and reduces the mortality risk for most patients in comparison with maintenance dialysis. Potential kidney transplant recipients must be carefully evaluated in order to detect and treat coexisting illnesses which may affect survival after transplantation. There are a few contraindications to transplantation that include: untreated current infection, active malignancy with short life expectancy, chronic illness with life expectancy of less than one year, poorly controlled psychosis, and active substance abuse. Most centers will retransplant carefully selected candidates however repeat transplant procedures are associated with higher failure rates.  

Professional Organizations

The Clinical Practice Committee of the American Society of Transplantation proposed that the presence of AIDS could be considered a contraindication to kidney transplant unless the following criteria were present. These criteria may be extrapolated to other solid organs:

- CD4 count > 200 cells/mm-3 for > 6 months
- HIV-1 RNA undetectable
- On stable anti-retroviral therapy > 3 months
- No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioses mycosis, resistant fungal infections, Kaposi’s sarcoma, or other neoplasm)
- Meeting all other criteria for transplantation

The National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (K/DOQI) has defined Chronic Kidney Disease (CKD) as a disorder lasting three or more months with either kidney damage defined by structural or functional abnormalities of the kidney with or without decreased estimated glomerular filtration rate (GFR), or a GFR of less than 60 mL/min per 1.73 m2. The K/DOQI workgroup also developed a classification for patients with CKD who are older than two years of age based upon the level of kidney function as follows:

- Stage 1 disease — Normal GFR (≥90 mL/min per 1.73 m2)
- Stage 2 disease — GFR between 60 and 89 mL/min per 1.73 m2
- Stage 3 disease — GFR between 30 and 59 mL/min per 1.73 m2
- Stage 4 disease — GFR between 15 and 29 mL/min per 1.73 m2
- Stage 5 disease — GFR of less than 15 mL/min per 1.73 m2 or end-stage renal disease (ESRD)

The British Renal Association clinical practice guidelines for kidney transplantation recommend the following:

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- Kidney transplantation should be the treatment of choice for patients with chronic kidney disease stage 5 who are considered fit for major surgery and for chronic immunosuppression.
- Patients should be predicted to have an increased life expectancy post-transplantation should be assessed for transplantation.
- Living donor transplantation should be considered the treatment of choice for all patients suitable for renal transplantation when there is an appropriate donor.
- Age is not a contra-indication to transplantation but age related co-morbidity is an important limiting factor.
- Obese patients (BMI >30 kg/m$^2$) present technical difficulties and are at increased risk of peri-operative complications. They should be screened rigorously for cardiovascular disease and each case considered individually. Although obesity is not an absolute contra-indication to transplantation, individuals with a BMI >40 kg/m$^2$ are less likely to benefit.

The American Society of Transplant Surgeons (ASTS), American Society of Transplantation (AST), United Network for Organ Sharing (UNOS) and American Society of Nephrology (ASN) convened to examine simultaneous liver-kidney transplantation (SLK). Directors from the 25 largest liver transplant programs along with speakers with recognized expertise attended. The purposes of this conference were to propose indications for SLK, to establish a prospective data registry and, most importantly, to recommend standard listing criteria for these patients. Scientific registry of transplant recipients data, and single center data regarding chronic kidney disease (CKD) and acute kidney injury (AKI) in conjunction with liver failure as a basis for SLK was presented and discussed. The consensus was that Regional Review Boards (RRB) should determine listing for SLK, as with other MELD exceptions, with automatic approval for: (i) End-stage renal disease with cirrhosis and symptomatic portal hypertension or hepatic vein wedge pressure gradient $\geq 10$ mm Hg (ii) Liver failure and CKD with GFR $\leq 30$ mL/min (iii) AKI or hepatorenal syndrome with creatinine $\geq 2.0$ mg/dL and dialysis $\geq 8$ weeks (iv) Liver failure and CKD and biopsy demonstrating $>30\%$ glomerulosclerosis or $30\%$ fibrosis. The RRB would evaluate all other requests to determine appropriateness.  

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<td><strong>CPT</strong></td>
<td><strong>Description</strong></td>
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<td>Renal allotransplantation, implantation of graft; with recipient nephrectomy</td>
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<td>50370</td>
<td>Removal of transplanted renal allograft</td>
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<td>50380</td>
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<td><strong>HCPCS</strong></td>
<td><strong>Description</strong></td>
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<td>S2152</td>
<td>Solid organ(s), complete or segmental, single organ or combination of organs; deceased or living donor (s), procurement, transplantation, and related complications; including: drugs; supplies;</td>
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hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and Rehabilitative services, and the number of days of pre- and post-transplant care in the global definition

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**References**


10/26/11 – New evidence review was conducted by the MCG Committee. The document was approved without revision.

June 2012 Update

58. McKesson InterQual Criteria for Procedures: Adult 2012 InterQual Transplantation, Renal; 2012.