Chapter 8: Monitoring Kidney Allograft Function

8.1: We suggest measuring urine volume (*2C*):
- **every 1–2 hours for at least 24 hours after transplantation *(2D)*;**
- **daily until graft function is stable. *(2D)***

8.2: We suggest measuring urine protein excretion, *(2C)* at least:
- **once in the first month to determine a baseline *(2D)*;**
- **every 3 months during the first year *(2D)*;**
- **annually, thereafter. *(2D)***

8.3: We recommend measuring serum creatinine, (*1B*) at least:
- **daily for 7 days or until hospital discharge, whichever occurs sooner *(2C)*;**
- **two to three times per week for weeks 2–4 *(2C)*;**
- **weekly for months 2 and 3 *(2C)*;**
- **every 2 weeks for months 4–6 *(2C)*;**
- **monthly for months 7–12 *(2C)*;**
- **every 2–3 months, thereafter. *(2C)***

8.3.1: We suggest estimating GFR whenever serum creatinine is measured, (*2D*) using:
- **one of several formulas validated for adults *(2C)*; or**
- **the Schwartz formula for children and adolescents. *(2C)***

8.4: We suggest including a kidney allograft ultrasound examination as part of the assessment of kidney allograft dysfunction. *(2C)*

GFR, glomerular filtration rate.

Background

Some tests need to be performed routinely to detect abnormalities that may lead to treatment or prevention of complications that are common in KTRs (Table 4). The frequency of screening is based on the incidence of the complication being screened, because there are no other data to determine the best interval for screening. Serum creatinine is easily measured and readily available in most laboratories. Screening tests for urine protein excretion include dipstick tests for total protein or albumin, as well as randomly collected 'spot' urine to measure protein-to-creatinine or albumin-to-creatinine ratios.

Rationale

- Detecting kidney allograft dysfunction as soon as possible will allow timely diagnosis and treatment that may improve outcomes.
- Urine output that is inappropriately low, or inappropriately high, is an indication of possible graft dysfunction.
- Serum creatinine and urine protein measurements are readily available and are useful for detecting acute and chronic allograft dysfunction.
- Ultrasound is relatively inexpensive and reasonably accurate for diagnosing treatable causes of kidney allograft dysfunction.

Urine volume

Urine volume is an easily-measured parameter of early kidney allograft function (120). The recovery of kidney function, measured as a decrease in serum creatinine and blood urea nitrogen, is generally preceded by an increase in urine volume (120). Rarely, excessive urine volume may indicate the presence of a saline diuresis or a water diuresis caused by tubular damage. In addition to its role in assessing early allograft dysfunction, measuring the urine volume is an important part of overall fluid and electrolyte management.

Urine protein excretion

Proteinuria is an early and sensitive marker of kidney damage in CKD (121). Many causes of proteinuria are potentially reversible with appropriate treatment (Table 5) (122), and detection of proteinuria can therefore improve graft outcomes (113,122–132). Patients with proteinuria generally have lower kidney function compared to patients without proteinuria (122,129). Proteinuria is also associated with mortality and CVD events in KTRs (130–132).

Proteinuria includes albuminuria as well as other proteins. The urinary excretion rate for albumin and total protein can be estimated from the ratio of albumin or total protein to creatinine concentration in a casual urine specimen (133–136). Creatinine excretion is higher in men than in women. Therefore, the values in the general population and cut-off values for abnormalities in urine albumin-to-creatinine ratio are lower for men than women (137,138 (Table 6). For details, see Kidney Disease Outcomes Quality Initiative (KDOQI) Guidelines for Chronic Kidney Disease, Part 5, Assessment of Proteinuria (www.kidney.org/professionals/kdoqi/guidelines_ckd/p5_lab_g5.htm; last accessed March 30, 2009).

Serum creatinine

Causes of kidney allograft dysfunction that require rapid intervention for treatment to be effective include acute rejection, obstruction, urine leak, vascular compromise and some recurrent diseases, for example focal segmental glomerulosclerosis (FSGS). These causes are more common in the first few days to weeks after kidney

Table 4: Routine screening after kidney transplantation

	Screening intervals by time after transplantation					
Screening test	1 week	1 month	2–3 months	4–6 months	7–12 months	>12 months
Creatinine[a]	Daily	2–3 per week	Weekly	Every 2 weeks	Monthly	Every 2–3 months
Urine protein[b]	.....Once.....		.....Every 3 months.....			Annually
Complete blood count[c]	Daily	2–3 per week	Weekly	.....Monthly.....		Annually
Diabetes[d]	.....Weekly.....		.....Every 3 months.....			Annually
Lipid profile[e]	–	–	Once	–	–	Annually
Tobacco use[f]	Prior to discharge		–	–	–	Annually
BKV NAT[g]	.....Monthly.....			.....Every 3 months.....		–
EBV NAT (seronegative)[h]	Once	.....Monthly.....		.....Every 3 months.....		–
Blood pressure, pulse, height, body weight	.....Each clinic visit.....					

BKV, BK polyoma virus; EBV, Epstein-Barr virus; NAT, nucleic acid testing.
[a]Serum creatinine.
[b]Urine total protein and/or urine albumin.
[c]Complete blood count including white blood count, hemoglobin and platelet counts.
[d]Screen for diabetes with fasting blood glucose, glucose tolerance test, or HbA_{1c} level.
[e]Lipid profile includes fasting cholesterol, LDL-C, HDL-C, and triglycerides.
[f]Screen for tobacco use.
[g]Screen for BKV using plasma NAT.
[h]Screen for EBV using plasma NAT in patients with no antibody to EBV at transplant.

transplantation than in subsequent months to years. Therefore, it is important to closely monitor kidney function early after transplantation.

Measurement of the serum creatinine concentration is a simple, inexpensive and universally available method for estimating GFR, and it is reliable for detecting acute changes of kidney function (142,143). The level of serum creatinine at year 1 after transplantation is a risk factor for subsequent outcomes, and may help guide care, for example the frequency of visits (144,145).

A gradual increase in serum creatinine after the first year may be due to acute rejection, but more often is caused by CAI, recurrence of the original kidney disease, or *de novo* kidney disease. Unfortunately, serum creatinine is less reliable for detecting chronic changes (over months to years) in kidney function.

As is true in the general population, measurement of GFR with inulin, iothalamate, iohexol or other suitable markers of GFR, either with urinary or plasma clearance techniques, provides the most accurate measure of allograft function in KTRs. Although these tests are appropriate for clinical use, the Work Group did not recommend their use in routine clinical practice due to cost, low patient acceptance, and lack of availability outside of academic medical centers. Measurement of cystatin C has also been used to monitor kidney function. The advantage of cystatin C is its independence from body weight. However, at present, there is a paucity of validation studies for cystatin C estimates of GFR in KTRs (146–148).

Formulas to estimate GFR have been tested in KTRs, but no formula has been consistently shown to be superior to any other formula (149–156). It is unlikely that these formulas will improve the ability of serum creatinine to estimate acute changes in kidney function since, in most formulas, the only component of the formula that changes significantly is serum creatinine. It is similarly unclear whether formulas improve the ability of serum creatinine to measure chronic changes in kidney

Table 5: Some causes of proteinuria after kidney transplantation

Persistent disease in the native kidneys
Allograft rejection and drug toxicity
Acute rejection
Thrombotic microangiopathy
CAI
Transplant glomerulopathy
***De novo* and recurrent glomerular diseases**
Minimal change disease
FSGS
IgA glomerulonephritis
Membranous glomerulonephritis
Membranoproliferative glomerulonephritis
Postinfectious glomerulonephritis
Thrombotic thrombocytopenic purpura
HUS
Vasculitis
Diabetic nephropathy
Systemic lupus erythematosus
Amyloidosis
Light- and heavy-chain deposition diseases

CAI, chronic allograft injury; FSGS, focal segmental glomerulosclerosis; HUS, hemolytic-uremic syndrome; IgA, Immunoglobulin A.

Table 6: Definitions of proteinuria and albuminuria

	Urine collection method	Normal	Microalbuminuria	Albuminiuria or clinical proteinuria
Total protein	24-h excretion	<300 mg/day (adults) <4 mg/m^2/h (children)	NA	≥300 mg/day (adults) ≥4 mg/m^2/h (children)
	Dipstick	<30 mg/dL (adults and children)	NA	≥30 mg/dL (adults and children)
	Spot protein-to-creatinine ratio	<200 mg/g (adults) <0.2 mg/mg (children 2 years or older) <0.5 mg/mg (<6–24 months old)	NA	≥200 mg/g (adults)
Albumin	24-h excretion	<30 mg/day	30–300 mg/day	>300 mg/day
	Albumin dipstick	<3 mg/dL	≥3 mg/dL	NA
	Spot albumin-to-creatinine ratio	<17 mg/g (men) <25 mg/g (women) <30 mg/g (children)	17–250 mg/g (men) 25–355 mg/g (women)	>250 mg/g (men) >355 mg/g (women)

NA, not applicable.
Reference values for urinary protein and albumin excretion in pediatric patients (139,140). To convert metric units to SI units, see Conversion Factors, p. Six.
Modified with permission (141).

transplant function, especially when serum creatinine may change due to changes in muscle mass due to an improved nutritional status after kidney transplantation (157–159).

Kidney allograft ultrasound examination

Many of the most common causes of allograft dysfunction, other than rejection, can be diagnosed by ultrasound. These include arterial occlusion, venous thrombosis, urinary obstruction, a urine leak (large fluid collection), compressing perinephric hematoma and arteriovenous fistula from a kidney biopsy (160–163). Ultrasound is also useful in guiding a kidney allograft biopsy, so it is often obtained at the time of biopsy. In the kidney allograft, mild to moderate calyceal distension can be normal, so a baseline ultrasound examination when kidney function is normal may be useful to compare to subsequent ultrasound examinations for allograft dysfunction.