Penn Medicine

Post Kidney Transplant Shared Care Model

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Why is shared care model important for kidney transplant recipients

- Kidney transplant recipients require unique medical care
- Multidisciplinary care is core to the successful outcome
- At transplant centers – post transplant coordinators, pharmacists, social workers and rest of the team along with the providers work closely
- The expertise of the transplant centers should be used as a critical resource for the long-term follow-up of renal transplant patients
- Role of Primary care physicians and referring nephrologists are of paramount importance for long term care of transplant recipients
- In order to simplify the logistics of following these complex patients, responsibilities in following different medical issues should be clearly defined

Medical Conditions Unique to Kidney Transplant Recipients

- Renal function
- Immunosuppression/therapeutic drug monitoring
- Cardiovascular disease Management
- Infectious Disease
- Malignancy

Early Post-Transplant Complications

- Surgical Complications
  - —Urological complications
  - —Peri-nephric fluid collection
  - —Renovascular complications

- Graft dysfunction
  - —Primary non-function
  - —Delayed Graft function
  - —Slow Graft function

Delayed Graft Function

Delayed graft function (DGF) is a common complication most frequently defined as the need for dialysis during the first post-transplant week

Incidence range 15-30% (around 20-23% in recent years)

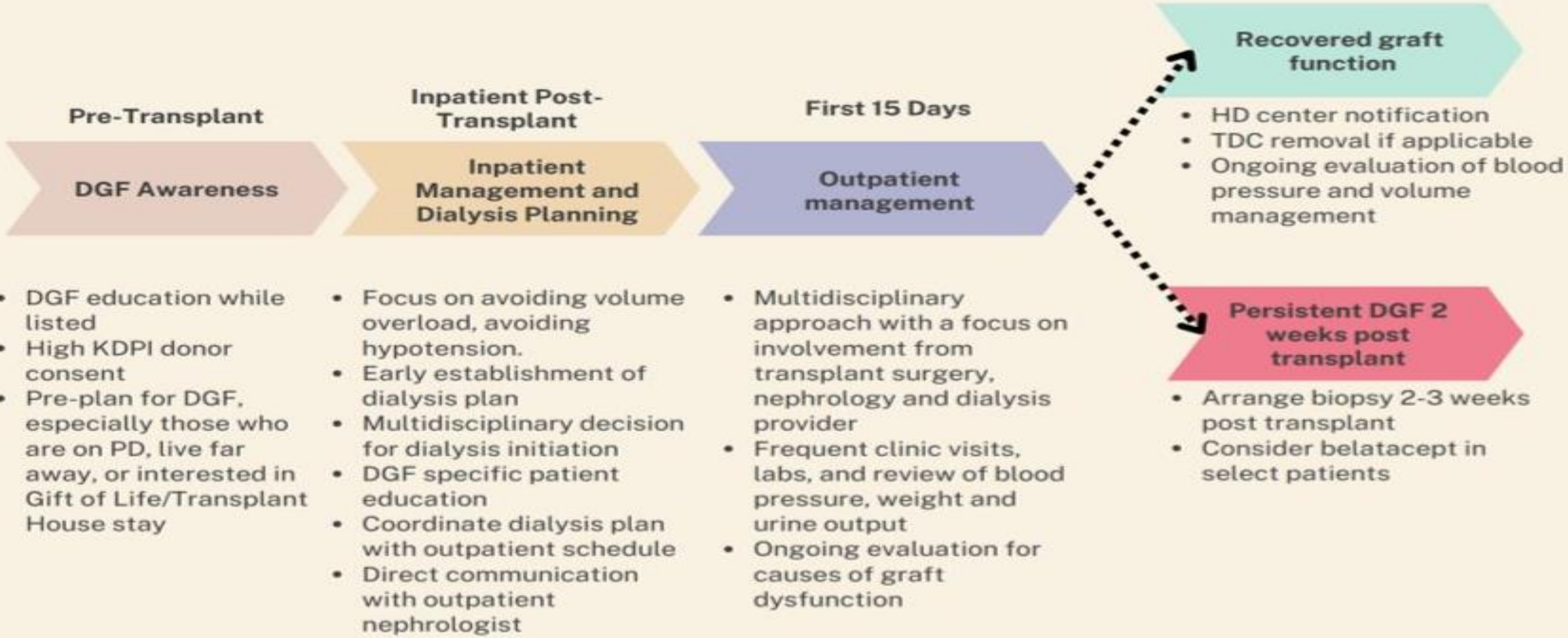
Risk Factors

- DCD donors
- CIT
- Recipient BMI
- Donor terminal creatinine

Impact of DGF

- Higher risk of rejection
- No difference in patient survival
- Graft survival is lower in the presence of acute rejection

DGF PATHWAY SUMMARY



DGF Clinic

Outpatient Management

Schedule

Clinic Schedule:

- Flexible provider scheduling but preferentially schedule patients with DGF on Mondays

Lab Schedule:

- M/W/F HD: Early lab on MWF
- T/Th/S HD: Monday and Thursday labs

Team

- Transplant Surgery Team
- Transplant Nephrology Team
- Post-Kidney Coordinators
- Post-Transplant Clinic MAs
- Transplant pharmacist
- Social worker
- Outpatient dialysis provider

General Management

Dialysis planning	Communicate plan regularly with primary nephrologist and/or nephrologist at PPMC.
BP	Consider holding blood pressure meds on AM of dialysis days aside from beta blockers in cases of atrial fibrillation. Patient to report weights, BP and UOP at least twice weekly.
Volume management	Consider diuretics on non dialysis days.
Electrolytes	Review dietary potassium and phosphorus restriction. Review phosphorus binders.
Anemia	ESAs to be managed at dialysis unit only. Assess for iron deficiency.

DGF Recovery
Communication with outpatient dialysis provider
Access care management: - Weekly flushes for PD catheters - HD catheters require weekly flushes and dressing changes - Removal of catheters when indicated
Ongoing patient education for weight and BP monitoring as they make more urine
At least twice weekly review of volume management/diuretic dosing/BP medications/medication dosing per GFR

Prolonged DGF (> 2 weeks)
Communication with primary nephrologist/PPMC
Consider repeat post void or renal ultrasound
Biopsy to be arranged at 2-3 weeks.
Belatacept to be considered on an individual basis in appropriate patient if anticipated prolonged DGF. (Discuss at weekly conference)

Recommendations for Collaborative Management - Renal Function

Surveillance recommendation provided by transplant center

- Management plan for renal function monitoring
- Management plan for monitoring of urinary protein excretion.
- Management plan for monitoring of blood pressure control, calcium and phosphorus abnormalities, anemia, hypoalbuminemia, acidosis, and lipid abnormalities

Referral/Consult transplant center

- Significant change in renal function
- New onset of significant proteinuria
- Significant increase in baseline proteinuria
- Interpretation and management following a kidney biopsy performed for any reason
- Referral for re-transplantation evaluation in patients with a failing allograft

Recommendations for Collaborative Management - Immunosuppression

Surveillance recommendations provided to Referring Providers

- Therapeutic drug monitoring schedule and goals
- Past and current side effects of immunosuppression experienced by the patient
- Any prior immunosuppression changes and rationale

Referral/Consult to Transplant Center

- Major surgery
- Treatment of new onset acute/chronic infections
- Transition of medications from oral to intravenous formulations
- The desire or occurrence of pregnancy
- Severe or opportunistic infection
- Changes in the medication regimen other than immunosuppression undertaken by other care providers should be discussed with or at least communicated to the Transplant Center, since other medication can significantly interfere with immunosuppressive medications. This particularly applies to medications that affect Cyp3A4 metabolism.

Common Drug Interactions with Immunosuppressive Agents

Table 1. Common Drug Interactions

Agent	Comment
Common Drugs That Increase CNI Level	
Erythromycin, clarithromycin	Potent inhibition of cytochrome P450 *Alternatives:* Azithromycin is an acceptable alternative in some cases, less impact on drug metabolism
Azole antifungals	Potent inhibition of cytochrome P450
Diltiazem, verapamil	Moderate inhibition of cytochrome P450 *Alternatives:* Nondihydropyridine calcium channel blockers or β-blockers
Protease inhibitors (eg, ritonavir, darunavir, indinavir)	Very potent inhibitors of metabolism *Alternatives:* nucleoside reverse-transcriptase inhibitors, non-nucleoside reverse-transcriptase inhibitors, or integrase inhibitors
Common Drugs That Decrease CNI Level	
Rifampin	Inducer of cytochrome P450
Rifabutin	Inducer of cytochrome P450
Carbamazepine	Inducer of cytochrome P450
Phenobarbital	Inducer of cytochrome P450

CVE in Post-Transplant

Risk for CVE is 3-5 times higher than general population; 10-20 times higher in HD patients

Incidence is around 4 per 100 patient-years

Fatal incident around 1.2 per 100 patient years

Common events- MI,CVA, angioplasties, CABG

Risk factors

- Prior cardiac event 4 -5 times
- DM more than 3 -4 times
- Smoking 2-3 times
- Obesity 2-3 times
- Multiple rejections 2 times
- Dialysis more than 2 years almost twice the risk
- Age > 45 years 50% higher risk

Mattos AM et al, Kidney Int 2006 70 757-764

Recommendations for Collaborative Management – Cardiovascular Disease

Surveillance recommendations to be provided to Referring Providers

- Fasting lipid profile goals
- Blood pressure goals
- Smoking history and goals for cessation
- Assessment of weight gain following transplant
- Diabetes management plan

Conditions in which Transplant Center consultation of CV disease is appropriate include the following

- Hyperlipidemia uncontrolled, with consideration of immunosuppression change
- Hypertension uncontrolled, with consideration of immunosuppression change
- New onset diabetes after transplant
- Uncontrolled diabetes with consideration of immunosuppression change
- Myocardial infarction
- Coronary artery disease requiring revascularization (CABG, angioplasty/stent)
- Cerebrovascular event
- Peripheral arterial disease requiring revascularization (bypass, angioplasty/stent)

Common infections associated with time since kidney transplantation.

Early Post-Transplant Infections 0–30 Days Post-Transplant	Period of Peak Immunosuppression 31–365 Days Post-Transplant	Late-Onset Infections >365 Days Post-Transplant
Nosocomial Infections • MDRO: MRSA, VRE, ESLB/CRE • *C. difficile* colitis • Surgical site infections • Urinary tract infection • Catheter-related bloodstream infections • Pneumonia **Donor-Derived Infections** • Atypical post-transplant course -Examples: LCMV, WNV, *T. cruzi*, HCV, Bacteremia, endemic mycoses **Recipient-Derived Infections** • Incubating or colonizing -Influenza, Pseudomonas, Aspergillus	**With Prophylaxis** • Polyomaviruses • HCV • *Cryptococcus neoformans* • *M. tuberculosis* • Strongyloides • Leishmania • PTLD **After Prophylaxis Stops** • Pneumocystis • Herpesviruses (CMV, HSV, VZV) • HBV • Listeria, Nocardia, Toxoplasmosis • Community-Acquired Infections -Urinary tract infection -Pneumonia -*C. difficile* colitis	**Opportunistic Infections** • When these occur, must consider why they are happening late • CMV • JC/PML • PTLD/EBV • Nocardia **Community-Acquired Infections** • West Nile Virus • Community-acquired Pneumonia • Urinary tract infections • Influenza • Aspergillus, atypical molds • Hepatitis B or C

Akansha Agrawal et al. CJASN doi:10.2215/CJN.15971020

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Prophylaxis Against Infections

PCP Prophylaxis for six months

- TMP-SMX SS daily
- Atovaquone 1500mg daily
- Dapsone 100mg daily

CMV Prophylaxis

- Valgancylovir
  - CMV +/+ 3 months
  - CMV -/+ 3 months
  - CMV +/- 6 months

Fungal Infection Prophylaxis

- Nystatin
- Fluconazole

Recommendations for Collaborative Management – Infectious Disease

Infectious disease: surveillance recommendations to referring providers

- Assessment of risk of CMV disease, prophylaxis strategy and duration, and monitoring strategy
- Assessment of risk of BK virus nephropathy and monitoring strategy
- Assessment of risk of EBV transmission/disease and monitoring strategy
- Prophylaxis strategies for other commonly encountered opportunistic infections such as pneumocystis carinii, candida albicans, and herpesvirus
- Prophylaxis, monitoring, and treatment strategies for hepatitis B, hepatitis C, and HIV when applicable
- Recommendations for vaccination for influenza/covid

Referral/Consult to Transplant Center

- Protracted diarrhea/gastrointestinal symptoms
- Recurrent UTIs
- Fever associated with renal dysfunction
- Fever associated with mental status changes
- CMV viremia or disease
- BK virus viremia, nephropathy, or viruria
- EBV viremia or disease
- Opportunistic infections (e.g. pneumocystis, herpes zoster, nocardiosis, West Nile virus, cryptosporidium)
- Newly diagnosed or progressive Hepatitis B, C, and HIV/TB

Malignancies seen with increased frequency in the post-transplant population

Skin cancer –particularly squamous cell carcinoma (SCC) involving sun exposed areas, but also basal cell carcinoma, melanoma, and Merkel cell

Oral cancers— pharynx, larynx, oral cavity

Urogenital cancers— vulvar, male and female anogenital areas, uterine cervix, urinary tract (especially in patients having received cumulative cyclophosphamide doses over 20 gms)

Renal cell carcinoma in multi-cystic kidney disease or multicystic transformation of contracted native kidneys

Hodgkin's and non-Hodgkin's lymphomas, including **post-transplant lymphoproliferative disorder (PTLD)**

Kaposi sarcoma

Hepatocellular carcinomas (HCC) generally, but not exclusively related to recipient infection with Hepatitis B or advanced hepatitis C.

Transplant Centers are increasingly dependent upon Primary Providers for the periodic assessment of malignancy risk.

Recommendations for Collaborative Management -Malignancy

Surveillance recommendations to referring providers

- Renal transplant recipients should be screened for solid organ malignancy in an age appropriate manner following the guidelines of the ACS for the general population.
- Due to the **significantly increased risk for skin cancer**, all patients should have a yearly skin examination and patients with a history of skin cancer should have follow-up more frequently as indicated.
- Patients who have received prior treatment with chemotherapeutic agents such as cyclophosphamide or who have a history of analgesic nephropathy are at **increased risk for urogenital malignancies.** Urologic evaluation should be performed in these recipients in all cases of new onset microhematuria.
- **Renal cell cancers** need to be kept in mind
- Lymphomas including **PTLD** should be considered in all individuals with clinical symptoms suggesting organ involvement.
- Hepatitis B carriers and Hepatitis C with advanced fibrosis—every 6 month abdominal ultrasound and serum alpha fetoprotein levels

Referral/Consult Transplant Center

- The occurrence of all cancers in the renal transplant recipient should be reported to the transplant center as soon as they are identified

What is Penn Transplant Institute protocol and what we share with providers

Post-Kidney Transplant Appointment Schedule

During Month 1:	• Initial post discharge appointments within the first week with surgical APP, transplant nephrology, and transplant pharmacy, and with surgical APP or surgeon at week 3. More frequent appointments with the various disciplines will be scheduled as clinically indicated
Month 2-6	• Monthly appointments with transplant nephrology team (nephrologist or APP), and with the surgeons and other disciplines as needed for active issues (at any time post-transplant)
Month 8:	• Appointment with Transplant Nephrologist or Transplant APP
Month 10:	• Appointment with Transplant Nephrologist or Transplant APP
Month 12:	• Appointment with Transplant Nephrologist
After Month 12:	• Patient resumes follow up with their local nephrologist, recommended follow up frequency every 3 months • Transplant center follow up every 6-12 months until 24 months, then every 12 months

Post-Transplant Lab Schedule

Responsible MD	Transplant Surgery	Transplant Nephrologist					
POD	**0-30**	**31-90**	**91-180**	**181-365**	**1-2 yrs.**	**2-3 yrs.**	**>3 yrs.**
Frequency	2x/wk	weekly	2x/mo	monthly.	Every 6-8 wks.	Every 8-10 wks.	Every 12 wks.
CBC	X	X	X	X	X	X	X
CMP	X	X	X	X	X	X	X
Tac or CyA	X	X	X	X	X	X	X
BK Virus PCR	at 30d	monthly	monthly	at 270d & 365d	at 18 mo.	at 2yr	
Lipid Screening	at 30d		at 180d	at 365d	annual	annual	annual
25-vit D	at 30d			at 365d	annual	annual	annual
HgbA1C		at 90d		at 365d	annual	annual	
UA	at 30d	at 90d	at 180d	at 365d	annual	annual	annual
Urine Prot/Cr ratio	at 30d	at 90d	at 180d	at 365d	annual	annual	annual
Urine Micro	at 30d	at 90d	at 180d	at 365d	annual	annual	annual
HIV quant PCR	28-56 days post-transplant						
HCV quant	28-56 days post-transplant						
HBV DNA quant	28-56 days post-transplant						

Maintenance Immunosuppression

For Tacrolimus based Regimen

Kidney alone transplant on prednisone maintenance:

Month 1	8-12 ug/L
Months 2-3	8-10 ug/L
Months 4-12	6-8 ug/L
Month 12 onward	5-7 ug/L

Kidney alone transplant, prednisone-free:

Month 1	8-12 ug/L
Months 2-6	8-10 ug/L
Months 7-12	6-8 ug/L
Month 12 onward	5-7 ug/L

Simultaneous Kidney Pancreas (SPK) transplant:

Months 1-3	8-12 ug/L
Months 4-6	8-10 ug/L
Months 6-8	6-8 ug/L
Month 12 onward	5-7 ug/L

For all cyclosporine-based products

First 6 months	175 - 250 ug/L
Months 6-12, if no rejection has occurred in first six months	125 - 175 ug/L
Month 12 onwards, if used in combination with MMF and prednisone	75-125 ug/L

Sample of Transition of Care to Referring Providers Communication:

Ms. Zz with h/o …..received living donor kidney transplant on ----;

CMV +/+ EBV +/+
Induction: Thymoglobulin
Post-Transplant complications:

Recommended target levels/doses for Ms. Zz based on tacrolimus being dosed every 12 hours

Time post-txp	tacrolimus level	MMF dose	Prednisone dose
6-12 months	6-8 ng/ml	500 mg twice a day	5 mg daily
> 12 months	5-7 ng/ml	500 mg twice a day	5 mg daily

Recommended frequency of local nephrology office visits and bloodwork post-txp

Time post-txp (mos)	Office visits	Blood work
6-12	every 4-8 wks	monthly
12-24	every 3 months*	every 6-8 weeks
24-60	every 3 months*	every 8-12 weeks
>60	every 6 months*	every 3 months

*include annual visit to kidney transplant program

We recommend the following general guidelines to optimize care of kidney transplant recipients:

Routine health screening per contemporary guidelines keeping in mind that kidney recipients are at increased risk for:
New onset diabetes
Cardiovascular disease
Cancer
Infections

Patients with known cardiovascular disease should have regular cardiology follow up
Target blood pressure <130/80
Target LDL < 100 mg/dl (patients with history of CAD/DM may require lower target, would defer to their cardiologist)
Dermatology follow up at least annually given increased skin cancer risk
Contact the transplant center if you are concerned about potential drug-drug interactions with Ms. Zz's immunosuppression (tacrolimus is metabolized via the cytochrome P450 system)

Vaccinations after the first post-transplant year
AVOID ALL LIVE/ACTIVE VACCINES
Flu vaccine (once a year)
Pneumonia vaccine (every 5 years)
Tetanus [TDap] (every 10 years)
Updated COVID vaccine per contemporaneous guidelines
Shingles (inactive vaccine)

Nationally Recognized

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