

Primary Care of the Solid Organ Transplant Recipient

FRANCESCA M. CIMINO, MD, *Uniformed Services University of the Health Sciences, Bethesda, Maryland*

KATHERINE A.M. SNYDER, MD, *Naval Hospital Bremerton, Bremerton, Washington*

The advancing science of transplantation has led to more transplants and longer survival. As a result, primary care physicians are more involved in the care of transplant recipients. Immunosuppressive therapy has significantly decreased rates of transplant rejection but accounts for more than 50% of transplant-related deaths, often due to infections and other risks related to long-term use. Cardiovascular disease is the leading cause of non-transplant-related mortality. Aggressive risk factor management is recommended for transplant recipients, including a blood pressure goal of less than 130/80 mm Hg and statin therapy in kidney, liver, and heart recipients. Fertility typically increases posttransplant, and female transplant recipients should avoid pregnancy for one year after surgery. The best contraceptive choice is usually an intrauterine device. Because of the increased risk of infection, patients should be tested for graft dysfunction or infection if suspicion arises. Testing should be coordinated with the transplant center. Malignancies are a common cause of death in transplant recipients, requiring careful attention to screening recommendations and informed discussions with patients. Family physicians should maintain an ongoing relationship with the transplant team to discuss medication changes and the risk of infection or graft rejection. (*Am Fam Physician.* 2016;93(3):203-210. Copyright © 2016 American Academy of Family Physicians.)

CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz Questions on page 176.

Author disclosure: No relevant financial affiliations.

Since 1988, more than 600,000 solid organ transplants have been performed in the United States, and approximately 130,000 patients are currently awaiting transplants.¹ Five-year survival rates after liver and kidney transplants are 64% and 70%, respectively, and heart and lung recipients have a five-year survival rate of more than 50%.¹ Because of the increasing number of surviving transplant recipients, care is gradually shifting to the primary care physician's office. This article focuses on the primary care of adults who have received solid organ transplants.

Medications

Immunosuppressive therapy accounts for more than 50% of transplant-related deaths, often due to infections and other risks related to long-term use.² Patients typically receive high doses of two or more medications immediately after transplantation, with subsequent tapering over the following months to years to minimize long-term adverse effects.

Medication classes that reduce the risk of graft rejection include calcineurin inhibitors, which inhibit an enzyme that stimulates

T lymphocytes; mammalian target of rapamycin inhibitors, which impede cell growth and proliferation; and purine synthesis inhibitors, which include azathioprine (Imuran), methotrexate, and the commonly used subclass of mycophenolic acid derivatives, which inhibit enzymes needed for the growth of T and B lymphocytes. Corticosteroids are often also used early after transplantation, but are tapered as quickly as possible.³ Most of the preferred immunosuppressive medications are metabolized through the cytochrome P450 3A4 pathway and can interact with other medications. Because transplant recipients receive multiple medications, primary care physicians should be mindful of polypharmacy when starting new drugs. *Table 1* reviews these medications, including adverse effects and examples of significant drug-drug interactions.^{4,5} Because of the extensive list of interactions, particularly with calcineurin inhibitors, changes to any medication should be discussed with the transplant team.

Posttransplant Disease Management

Cardiovascular disease and renal failure are the leading causes of posttransplant morbidity and mortality independent of graft

Table 1. Posttransplant Immunosuppressive Medications and Drug Interactions

Medication class	Common adverse effects	Substances that increase concentration (not fully inclusive)*	Substances that decrease concentration*
Calcineurin inhibitors (e.g., cyclosporine [Sandimmune], tacrolimus [Prograf])	Hyperkalemia, hypertension, nephrotoxicity, neurotoxicity (e.g., headaches, tremors, neuropathy, seizures) Cyclosporine: dyslipidemia, gingival hyperplasia Tacrolimus: diabetes mellitus	Aminoglycosides Amphotericin B Antifungals: fluconazole (Diflucan), itraconazole (Sporanox), ketoconazole Cardiac medications: amiodarone Contraceptives: ethinyl estradiol Diuretics: spironolactone (hyperkalemia) Fluoroquinolones (primarily ofloxacin; ciprofloxacin and levofloxacin [Levaquin] often used safely) Grapefruit and grapefruit juice Macrolides (erythromycin more than clarithromycin [Biaxin]) Metronidazole (Flagyl) Nondihydropyridine calcium channel blockers: diltiazem, verapamil Nonsteroidal anti-inflammatory drugs (can increase nephrotoxicity) Pineapple and papaya (inhibit cyclosporine metabolism) Pomegranates and pomegranate juice Warfarin (Coumadin)	Antacids Antibiotics: nafcillin, rifampin Anticonvulsants: carbamazepine (Tegretol), phenytoin (Dilantin) Cholestyramine (Questran) Loperamide (Imodium) Supplements: echinacea (may cause organ rejection), St. John's wort Valproic acid (Depakene)
Mammalian target of rapamycin inhibitors (e.g., sirolimus, everolimus)	Dyslipidemia, hepatic artery thrombosis, myelosuppression, poor wound healing, pulmonary fibrosis, rash, ulcerations	Ciprofloxacin Linezolid (Zyvox; increased myelosuppression) Macrolides (erythromycin more than clarithromycin)	Rifampin
Purine synthesis inhibitors (e.g., azathioprine [Imuran], mycophenolate [Cellcept], mycophenolic acid [Myfortic])	Azathioprine: cholestatic hepatitis Mycophenolate/mycophenolic acid: bone marrow suppression, gastrointestinal issues (e.g., abdominal pain, diarrhea, gastritis, nausea)	Linezolid Valganciclovir (Valcyte; increased myelosuppression)	Allopurinol can increase levels to toxic levels (especially azathioprine) Rifampin

*—All immunosuppressive medications listed are metabolized through the cytochrome P450 3A4 pathway; thus, medications that inhibit this pathway will increase circulating levels of those drugs, and those that induce that pathway will decrease levels.

Information from references 4 and 5.

rejection.⁴ Increased cardiovascular risk is thought to be mediated by increased rates of hypertension, diabetes mellitus, hyperlipidemia, and obesity. *Table 2* summarizes risk factors and provides recommendations for screening and treatment of posttransplant systemic diseases.⁴⁻⁸

HYPERTENSION

The Eighth Joint National Committee did not specifically address the target blood pressure range for solid organ transplant recipients.⁹ The goal suggested by transplant experts is less than 130/80 mm Hg.^{4,6} The choice of antihypertensive therapy depends on patient comorbidities and the immunosuppressive regimen. There is only limited evidence supporting the use of specific

antihypertensive classes, and transplant experts do not strongly recommend any class for first-line therapy.

Calcium channel blockers (CCBs) may counteract the vasoconstrictive effects of calcineurin inhibitors to control blood pressure and reduce nephrotoxicity. A Cochrane review found 17 randomized trials comparing CCBs with placebo or no treatment in 1,255 patients.¹⁰ Based on low-quality evidence, it concluded that CCB use may reduce the risk of graft loss (68 vs. 90 per 1,000 over a median of one year) but has no effect on overall mortality or acute graft rejection. Dihydropyridine CCBs are less likely to interact with calcineurin inhibitors, and the Cochrane review concluded that they may have a more favorable effect on serum creatinine

Table 2. Posttransplant Care of Metabolic Diseases

Condition	Screening intervals	Treatment considerations*	Treatment goals*
Chronic kidney disease	Annually (minimum): GFR and spot urine protein (or albumin)-to-creatinine ratio Increase frequency in patients with rapid decline or GFR < 60 mL per minute per 1.73 m ²	Consider renal-sparing maintenance immunosuppressives	—
Diabetes mellitus	Kidney and liver recipients: every three months for first year, then annually; after substantially increasing dose of calcineurin inhibitor, mammalian target of rapamycin inhibitor, or cyclosporine (Sandimmune)	Oral hypoglycemics and insulin are safe Kidney recipients: aspirin for primary prevention of cardiovascular disease	Kidney recipients: A1C < 7% to 7.5% Liver recipients: A1C < 7%
Hyperlipidemia	Kidney and heart recipients: not specified Liver recipients: annually	Statin doses are generally lower than in general population; 50% reduction when used with cyclosporine Liver recipients: isolated triglycerides may be treated initially with fish oil (1 g two times daily to 4 g daily as tolerated)	Kidney recipients: triglycerides < 500 mg per dL (5.7 mmol per L) Liver recipients: low-density lipoprotein < 100 mg per dL (2.59 mmol per L)
Hypertension	Every appointment	Use caution with diltiazem and verapamil (drug interactions)	Kidney and liver recipients: < 130/80 mm Hg
Osteopenia/osteoporosis	Heart recipients: one year after transplant; then annually if receiving corticosteroids or bisphosphonates; if osteopenic, repeat every two years; if normal, repeat every three years Kidney recipients: measure calcium, PTH, phosphorus, and vitamin D levels at intervals determined by baseline values, level of pre-transplant disease, and renal function; GFR > 30 mL per minute per 1.73 m ² , check bone mineral density three months posttransplant if receiving corticosteroids or if patient has osteoporosis risk factors Liver: initially, then annually for first five years posttransplant; if osteopenic, every two to three years if normal	Kidney recipients: consider vitamin D, calcitriol (Rocaltrol), alfacalcidol, or bisphosphonates if GFR > 30 mL per minute per 1.73 m ² and low bone mineral density; manage abnormalities in calcium, phosphorus, vitamin D, and PTH levels as in the pretransplant population Liver recipients: bisphosphonate treatment for patients with osteoporosis or osteopenia with other risk factors	Heart and liver recipients: serum 25-hydroxyvitamin D levels > 30 ng per mL (75 nmol per L)

GFR = glomerular filtration rate; PTH = parathyroid hormone.

*—Treatment considerations and goals include specific recommendations if targets are different from the general population.

Information from references 4 through 8.

levels and glomerular filtration rate.¹⁰ However, nondihydropyridine CCBs may be used if therapeutic levels of calcineurin inhibitors are monitored.^{4,6,10} Use of a nondihydropyridine CCB can reduce dosage requirements and therefore the cost of calcineurin inhibitors.^{6,7} Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are first-line agents in kidney recipients if urinary protein excretion exceeds 1 g per day, but their use can cause increased serum creatinine levels, hyperkalemia, and anemia.⁷ Thiazide diuretics are recommended in kidney recipients to counteract the sodium-related effects of calcineurin inhibitors. However, loop and thiazide diuretics should be used with caution in liver recipients.^{4,7} Kidney recipients with resistant

hypertension should be referred back to the transplant center to rule out allograft vascular compromise and complications related to the native kidneys, which are not typically removed during transplant surgery.⁷

HYPERLIPIDEMIA

Statins are the preferred agent to treat hyperlipidemia and reduce cardiovascular risk in solid organ transplant recipients. The American Association for the Study of Liver Disease/American Society of Transplantation recommends a low-density lipoprotein goal of less than 100 mg per dL (2.59 mmol per L) in liver recipients.⁴ The Kidney Disease Improving Global Outcomes and International Society of Heart and Lung

Transplant Care

Transplantation guidelines recommend universal statin therapy in kidney and heart recipients.^{5,8} Initial statin doses in all solid organ transplant recipients are lower than those in the general population because of potential interactions with calcineurin inhibitors.^{5,8}

All of the recommendations above are based on expert opinion. A 2014 Cochrane review of 22 studies with 3,465 patients found that statin therapy had inconsistent or uncertain effects on all-cause and cardiovascular mortality, major cardiovascular events, and fatal or nonfatal myocardial infarctions in kidney recipients.¹¹ Evidence favoring statin treatment is more robust in heart recipients; statin therapy in first-time recipients reduces rates of mortality and allograft rejection with hemodynamic compromise at one year,¹² reduces cardiac allograft vasculopathy, and improves long-term outcomes regardless of lipid levels.⁵

CHRONIC KIDNEY DISEASE

Non-kidney solid organ transplant recipients have higher posttransplant rates of chronic kidney disease. Strategies recommended to reduce disease progression mirror those in the general population: blood pressure and glucose control, and use of medications that block the renin-angiotensin-aldosterone system. Additionally, transplant centers may decrease calcineurin inhibitor doses, potentially transitioning to an inhibitor-free regimen to preserve renal function.^{4,5}

DIABETES

Diabetes can be preexisting or can occur for the first time posttransplant. All major transplant societies recommend screening and treatment, in accordance with guidelines from the American Diabetes Association.^{4,5,7} The target A1C is less than 7% in most transplant recipients.^{4,5,7} Insulin is typically required, but oral hypoglycemic agents can also be used with the same restrictions for comorbid conditions as in the general population.^{4,7} The use of thiazolidinediones has not been proven safe in liver recipients.⁴ The risk of new-onset diabetes is highest in the first three months after transplantation. Although there is no consistent evidence that new-onset diabetes resolves as immunosuppressive therapy is tapered, glycaemic control often improves with time.^{4,5,7}

OBESITY

Obesity (body mass index greater than 30 kg per m²) occurs in roughly 20% to 30% of liver and kidney recipients who were not obese before the transplant.^{4,13} Improved appetite after transplantation and medication adverse effects are likely contributing factors.⁴ Lifestyle

Table 3. Tests to Monitor for Transplant Rejection

<i>Transplant type</i>	<i>Typical graft function assessment</i>
Heart	Endomyocardial biopsy
Kidney	Urine protein levels (total, protein-to-creatinine ratio, albumin-to-creatinine ratio), serum creatinine level (to calculate glomerular filtration rate)
Liver	Transaminase, bilirubin, and alkaline phosphatase levels
Lung	Bronchoscopy with transbronchial biopsies, pulmonary function testing

Information from references 4, 5, 7, and 18.

modifications remain the cornerstone of therapy, but bariatric surgery is not contraindicated.^{4,7}

BONE DISEASE

Osteopenia and osteoporosis are common before transplantation. Multiple factors, including corticosteroid therapy, cause bone mineral density to decrease and fracture risk to increase in the immediate posttransplant period.^{14,15} Although transplant experts use standard definitions for osteoporosis and osteopenia based on bone mineral density, fracture risk in solid organ transplant recipients does not correlate directly with these values.^{5,15,16}

Evidence regarding fracture risk reduction with any agent is inconsistent.^{15,17} Kidney recipients can have abnormal serum levels of phosphorus, parathyroid hormone, and vitamin D. Treatment for these conditions should be similar to that in the pretransplant period. In kidney recipients with osteoporosis, bisphosphonate therapy is recommended only in the first year after the transplant. Bone biopsy should be considered in kidney recipients because of their increased risk of adynamic bone disease, which is worsened by bisphosphonate use.¹⁵ Heart recipients should receive bisphosphonates for the first year after transplant to prevent bone loss.⁵ Bisphosphonate therapy is also recommended for liver recipients who have osteoporosis or osteopenia with risk factors.⁴

Graft Dysfunction

Graft dysfunction is often first noted through routine screening tests or surveillance biopsies. Screening for rejection or other graft complications is site-specific and based on individual patient characteristics, including time from transplant and stability of previous testing.⁴ The transplant team should be notified immediately if there is any concern for graft dysfunction or rejection. *Table 3* presents typical screening tests according to transplant type.^{4,5,7,18}

Table 4. Comparison of Contraceptives for Transplant Recipients

<i>Contraceptive</i>	<i>Advantages</i>	<i>Disadvantages</i>
Combined oral contraceptives	Widely available and affordable	Failure rate for typical use is 8%; estrogen-containing contraceptives may increase blood levels of corticosteroids, cyclosporine (Sandimmune), tacrolimus (Prograf), and sirolimus
Intrauterine devices	No increased risk of infection; no change in effectiveness for immunosuppressed patients; no drug interactions; does not contain estrogen	—
Intravaginal ring and combined hormonal contraceptive patch	Avoids first-pass effect; may decrease risk of drug interactions with estrogen; intravaginal ring has lower total daily dose of estrogen	Complications related to estrogen-containing contraceptives; increased circulating levels of estrogen with patch
Medroxyprogesterone (Provera)	Avoids first-pass effect; does not contain estrogen	U.S. Food and Drug Administration boxed warning for bone health combined with propensity for decreased bone mineral density
Subdermal implants	Fewer bone density effects compared with medroxyprogesterone; does not contain estrogen	—

Information from references 19 through 21.

Reproductive and Sexual Health

Transplant recipients often struggle with infertility, erectile dysfunction, and other reproductive and sexual concerns before and after the transplant. Fertility generally improves post-transplant.^{19,20} The National Transplantation Pregnancy Registry follows pregnancy outcomes, and patients are encouraged to register; enrollment forms are available at <http://www.ntpr.giftoflifeinstitute.org>.

Male transplant recipients often have incomplete recovery of gonadal function, but are still able to father a child. Erectile dysfunction can be treated with phosphodiesterase-5 inhibitors.^{4,5,7} The risk of pregnancy complications is not increased when the father is a kidney recipient. Men may wish to bank sperm before they use mammalian target of rapamycin inhibitors.⁷

Pregnancy during the 12 months following transplantation is associated with an increased risk of preterm delivery and graft dysfunction, rejection, or loss.^{19,21} Reliable contraception should be used before the transplant because ovulation can occur as early as one month posttransplant. The use of an intrauterine device avoids interactions with medications, does not increase the risk of infection, and is not affected by typical immunosuppressive therapies. For these reasons, physicians should encourage female transplant recipients to strongly consider an intrauterine device for contraception.^{20,21} The medical eligibility criteria for contraceptive use from the Centers for Disease Control and Prevention include specific recommendations for contraceptive types during the first two years after solid organ transplantation.²² A comparison of contraceptive methods specific to transplant recipients is presented in *Table 4*.¹⁹⁻²¹

Transplant centers should be notified before attempts to conceive; this allows for evaluation of

graft function and adjustment of immunosuppressive regimens, if needed. Ideally, patients should not have experienced graft rejection within the past year; should have stable graft function, no acute infections, and controlled comorbidities; and should be on a stable immunosuppressive regimen before conceiving.^{4,7,19} Certain immunosuppressive agents should be discontinued before pregnancy because of the increased risk of fetal compromise. Mycophenolic acid compounds have about a 25% risk of birth defects, and mammalian target of rapamycin inhibitors increase the risk of preterm delivery, decreased fetal weight, and delayed skeletal ossification.^{7,19,23} Azathioprine, cyclosporine (Sandimmune), and tacrolimus (Prograf) have not been shown to increase the risk of birth defects.¹⁹

Transplant recipients have a high risk of miscarriage, gestational hypertension, preeclampsia, gestational diabetes, and fetal complications such as prematurity and low birth weight. They typically require consultation or management by obstetricians and maternal-fetal medicine subspecialists. Although cesarean deliveries are not routinely recommended, they are performed more often in kidney (44%) and liver (57%) recipients.¹⁹

Most transplant recipients may safely breastfeed their infants. The benefits of breastfeeding while receiving corticosteroids, cyclosporine, tacrolimus, or azathioprine outweigh the risks of drug exposure. Physicians should monitor infant serum drug levels for the first few weeks of life, and should recommend discontinuing breastfeeding only if measurable levels are detected. Breastfeeding is not recommended for mothers receiving mycophenolic acid (Myfortic), sirolimus, everolimus, or belatacept (Nulojix); these agents have limited safety data, and mycophenolic acid is known to increase the risk of fetal malformations from in utero exposure.²³

Table 5. Treatment and Prophylaxis for Opportunistic Infections in Transplant Recipients

<i>Infection</i>	<i>Treatment</i>	<i>Prophylaxis</i>
CMV	Reduction of immunosuppressive agents likely required	Ganciclovir (Cytovene) or valganciclovir (Valcyte) for three months posttransplant except in CMV-negative recipient/CMV-negative donor pairs and for six weeks after treatment with T lymphocyte-depleting antibody
Epstein-Barr virus	Reduction of immunosuppressive agents	—
Fungal infections	Antifungals and reduction of immunosuppressive agents	Liver recipients (high risk of infection): invasive <i>Candida</i> prophylaxis with fluconazole (Diflucan), itraconazole (Sporanox), caspofungin (Cancidas), or amphotericin B for one to three months posttransplant and one month after treatment with T lymphocyte-depleting antibody Kidney and heart recipients: oral and esophageal <i>Candida</i> prophylaxis with oral clotrimazole lozenges, nystatin, or fluconazole for one to three months posttransplant or one month after treatment with T lymphocyte-depleting antibody
Herpes simplex virus and VZV	Superficial infections: oral antivirals until lesions resolve Disseminated or systemic infections: intravenous antivirals and reduction of immunosuppressive agents until response, then transition to oral agents to complete 14- to 21-day course	Susceptible patients should receive prophylaxis after exposure to active VZV with VZV immune globulin (within 96 hours) or oral antivirals (after 96 hours)
<i>Pneumocystis jiroveci</i>	High-dose TMP/SMX with reduction in immunosuppressive agents for at least 14 days; corticosteroids may be used as adjunct in patients with significant hypoxia	TMP/SMX posttransplant (duration depends on organ; heart: unspecified; kidney: three to six months; liver: six to 12 months) Alternatively, can use dapsone or atovaquone (Mepron) Kidney recipients: six weeks during and after treatment for acute rejection
Tuberculosis	Standard treatment regimen; rifampin can decrease levels of calcineurin and mammalian target of rapamycin inhibitors	Consider in patients with latent tuberculosis, intensified immunosuppression, diabetes mellitus, or CMV, <i>P. jiroveci</i> , <i>Nocardia</i> , or fungal coinfections; isoniazid is preferred prophylactic agent

CMV = cytomegalovirus; TMP/SMX = trimethoprim/sulfamethoxazole; VZV = varicella zoster virus.

Information from references 4, 5, and 7.

Infection

Immunocompromised patients have an increased vulnerability to common and opportunistic pathogens. Typical treatment and prophylactic regimens for opportunistic infections in transplant recipients are summarized in Table 5.^{4,5,7} Treatment plans are best determined in consultation with the transplant center.

Preventive Care

Table 6 summarizes prevention strategy recommendations for transplant recipients.^{4,5,7,24-30}

CANCER SCREENING

Malignancy rates are higher in all transplant recipients.²⁴ The incidence of the most common cancers—colon, lung, breast, and prostate—are twofold higher than that in the general population.³¹ The risk of other cancers, including Kaposi sarcoma, non-Hodgkin lymphoma, nonmelanomatous skin cancers, and cancers related to viral infections, is increased as much as 20-fold.^{31,32}

Survival rates among transplant recipients who develop secondary cancers are often less than 10% over five years.³³ Most of the currently accepted guidelines for the general population do not specifically address cancer screening in transplant recipients.^{34,35}

Screening recommendations for breast, prostate, and colon cancers in transplant recipients mirror guidelines from the U.S. Preventive Services Task Force.^{34,35} Because cervical cancer is mediated by an oncogenic virus, some experts have debated more frequent surveillance, and the American Cancer Society recommends that physicians consider this on a case-by-case basis; however, there is no rigorous evidence to support this practice.^{34,35} Physicians should consider the patient's comorbidities and life expectancy, and have informed discussions with their patients.³³

Nonmelanomatous squamous cell and basal cell skin cancers are the most common malignancies in transplant recipients. Squamous cell cancers tend to develop at a younger age, are typically more aggressive, and

Table 6. Prevention Strategies for Transplant Recipients

Foodborne illness

Patients receiving transplant medications have increased susceptibility to foodborne pathogens and should consider following a low-microbial diet.²⁴

Unpasteurized dairy products (e.g., certain soft cheeses, cheeses with molds), undercooked and delicatessen meats, unwashed fruits and vegetables, sprouts, and raw honey should be avoided.

A handout on food safety for transplant recipients is available at <http://www.fda.gov/Food/FoodborneIllnessContaminants/PeopleAtRisk/ucm312570.htm>.

Immunizations

Age-appropriate vaccinations should be up to date before transplantation.

Live vaccines are allowable up to four weeks before transplant.

Inactivated vaccines are allowable up to two weeks before transplant.

Inactivated vaccines can be administered two weeks after transplant.

Most live vaccines are not safe after transplant.

Inactivated influenza vaccine is recommended annually.

Immunocompromised adults should receive 13-valent pneumococcal conjugate vaccine (Pneumovax 13), followed by 23-valent pneumococcal polysaccharide vaccine (Pneumovax) no earlier than eight weeks later.

Oral health care

Endocarditis prophylaxis is not necessary in transplant recipients unless there is an underlying cardiac condition that increases the risk of bacteremia.

Heart recipients showing any evidence of graft valvulopathy have an increased risk of valvular dysfunction and poorer outcomes if they acquire endocarditis; thus, prophylaxis is recommended for these patients before invasive dental procedures.

Tobacco use

Transplant recipients are at higher risk of tobacco-related morbidity and graft loss; thus, patients who use tobacco should be advised to quit.

Nicotine-replacement products and medications such as bupropion (Zyban) and varenicline (Chantix) are safe in these patients, but have not been studied for differences in effectiveness compared with the general population.

Travel

Transplant recipients should consider avoiding international travel, if possible, for six months posttransplant.

Travel should be avoided to countries where inability to obtain immunizations (e.g., for yellow fever or varicella) would put patients at risk.

Prophylactic agents for malaria do not interact significantly with mammalian target of rapamycin inhibitors, purine synthesis inhibitors, or corticosteroids.

Chloroquine (Aralen), mefloquine, and doxycycline may increase calcineurin inhibitor levels; atovaquone/proguanil (Malarone) does not.

Travelers should carry medications for traveler's diarrhea (fluoroquinolones preferred) and follow recommended guidelines on food and water intake.

Information from references 4, 5, 7, and 24 through 30.

metastasize more often.^{32,36} The incidence in the United States and western Europe increases from 10% to 27% at 10 years posttransplant to 40% to 60% at 20 years.³⁶ The National Comprehensive Cancer Network recom-

mends aggressive treatment, even for precancerous lesions such as actinic keratosis, and a low threshold for biopsy in any suspicious lesion.³⁷ Patients should be referred to a dermatologist within one year of the transplant and should be screened for skin cancer at least annually. Physicians should counsel patients to avoid sun exposure and to mitigate risk with appropriate clothing and sunscreen.³⁷

Data Sources: We conducted an Ovid search of all publications with the keywords solid organ transplantation, primary care, immunizations, screening, pregnancy, contraception, and rejection. In addition, we searched the Cochrane database, the National Guideline Clearinghouse, PubMed, and Clinical Queries. Most of our resources are meta-analyses, evidence-based guidelines, and subtopic-specific review articles. Search dates: May 2012, September and October 2014, and March and October 2015.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Navy, Department of Defense, or the U.S. government.

The Authors

FRANCESCA M. CIMINO, MD, is an active-duty family physician in the U.S. Navy and an assistant clinical professor at the Uniformed Services University of the Health Sciences, Bethesda, Md.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	References
A blood pressure goal of less than 130/80 mm Hg is recommended for all liver and kidney recipients.	C	4, 6
Statin therapy is recommended for all solid organ transplant recipients.	C	4, 5, 8
Pregnancy should be delayed for one year posttransplant.	C	4, 5, 7, 19, 21
Solid organ transplant recipients should be counseled about avoiding tobacco.	C	4, 7
Solid organ transplant recipients should be educated about sun avoidance and protection and evaluated by a dermatologist annually, starting within the first year posttransplant.	C	36, 37

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort>.

KATHERINE A.M. SNYDER, MD, is an active-duty family physician in the U.S. Navy. At the time the article was written, she was chief resident at Naval Hospital Bremerton, Wash.

Address correspondence to Francesca M. Cimino, MD, 4301 Jones Bridge Rd., Bethesda, MD 20814 (e-mail: francesca.m.cimino.mil@mail.mil). Reprints are not available from the authors.

REFERENCES

1. U.S. Dept. of Health and Human Services. Organ Procurement and Transplant Network. National data. <http://optn.transplant.hrsa.gov/converge/latestData/step2.asp>. Accessed October 1, 2014.
2. The U.S. Multicenter FK506 Liver Study Group. A comparison of tacrolimus (FK 506) and cyclosporine for immunosuppression in liver transplantation. *N Engl J Med*. 1994;331(17):1110-1115.
3. Pascual J, Zamora J, Galeano C, Royuela A, Quereda C. Steroid avoidance or withdrawal for kidney transplant recipients. *Cochrane Database Syst Rev*. 2009;(1):CD005632.
4. Lucey MR, Terrault N, Ojo L, et al. Long-term management of the successful adult liver transplant: 2012 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Liver Transpl*. 2013;19(1):3-26.
5. Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29(8):914-956.
6. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. *Kidney Int Suppl*. 2012;2(5):337-414.
7. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Transplant*. 2009;9(suppl 3):S1-S155.
8. Kidney Disease: Improving Global Outcomes (KDIGO) Lipid Work Group. KDIGO clinical practice guideline for lipid management in chronic kidney disease. *Kidney Int Suppl*. 2013;3(3):259-305.
9. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8) [published correction appears in *JAMA*. 2014;311(17):1809]. *JAMA*. 2014;311(5):507-520.
10. Cross NB, Webster AC, Masson P, O'Connell PJ, Craig JC. Antihypertensive treatment for kidney transplant recipients. *Cochrane Database Syst Rev*. 2009;(3):CD003598.
11. Palmer SC, Navaneethan SD, Craig JC, et al. HMG CoA reductase inhibitors (statins) for kidney transplant recipients. *Cochrane Database Syst Rev*. 2014;(1):CD005019.
12. Mehra MR, Raval NY. Metaanalysis of statins and survival in de novo cardiac transplantation. *Transplant Proc*. 2004;36(5):1539-1541.
13. Friedman AN, Miskulin DC, Rosenberg IH, Levey AS. Demographics and trends in overweight and obesity in patients at time of kidney transplantation. *Am J Kidney Dis*. 2003;41(2):480-487.
14. Hay JE. Osteoporosis in liver diseases and after liver transplantation. *J Hepatol*. 2003;38(6):856-865.
15. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). *Kidney Int Suppl*. 2009;(113):S1-S130.
16. Hardinger KL, Ho B, Schnitzler MA, et al. Serial measurements of bone density at the lumbar spine do not predict fracture risk after liver transplantation. *Liver Transpl*. 2003;9(8):857-862.
17. Palmer SC, McGregor DO, Strippoli GFM. Interventions for preventing bone disease in kidney transplant recipients. *Cochrane Database Syst Rev*. 2007;(3):CD005015.
18. Martinu T, Chen DF, Palmer SM. Acute rejection and humoral sensitization in lung transplant recipients. *Proc Am Thorac Soc*. 2009;6(1):54-65.
19. Deshpande NA, Coscia LA, Gomez-Lobo V, Moritz MJ, Armenti VT. Pregnancy after solid organ transplantation: a guide for obstetric management. *Rev Obstet Gynecol*. 2013;6(3-4):116-125.
20. Krajewski CM, Geetha D, Gomez-Lobo V. Contraceptive options for women with a history of solid-organ transplantation. *Transplantation*. 2013;95(10):1183-1186.
21. Patel PR, Schreiber CA. Controversies in family planning: contraceptive counseling in the solid organ transplant recipient. *Contraception*. 2013;87(2):138-142.
22. Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use, 2010: Adapted from the World Health Organization Medical Eligibility Criteria for Contraceptive Use, 4th edition. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5904a1.htm?cid=rr5904a1_e. Accessed November 6, 2014.
23. Thiagarajan KM, Arakali SR, Mealey KJ, et al. Safety considerations: breastfeeding after transplant. *Prog Transplant*. 2013;23(2):137-146.
24. Kasiske BL, Vazquez MA, Harmon WE, et al.; American Society of Transplantation. Recommendations for the outpatient surveillance of renal transplant recipients. *J Am Soc Nephrol*. 2000;11(suppl 15):S1-S86.
25. Lund BM, O'Brien SJ. The occurrence and prevention of foodborne disease in vulnerable people. *Foodborne Pathog Dis*. 2011;8(9):961-973.
26. Rubin LG, Levin MJ, Ljungman P, et al.; Infectious Diseases Society of America. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host [published correction appears in *Clin Infect Dis*. 2014;59(1):144]. *Clin Infect Dis*. 2014;58(3):e44-e100.
27. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group [published correction appears in *Circulation*. 2007;116(15):e376-e377]. *Circulation*. 2007;116(15):1736-1754.
28. Corbett C, Armstrong MJ, Neuberger J. Tobacco smoking and solid organ transplantation. *Transplantation*. 2012;94(10):979-987.
29. Stead LF, Perera R, Bullen C, et al. Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev*. 2012;(11):CD000146.
30. Kotton CN, Ryan ET, Fishman JA. Prevention of infection in adult travelers after solid organ transplantation. *Am J Transplant*. 2005;5(1):8-14.
31. Engels EA, Pfeiffer RM, Fraumeni JF Jr, et al. Spectrum of cancer risk among US solid organ transplant recipients. *JAMA*. 2011;306(17):1891-1901.
32. Kasiske BL, Snyder JJ, Gilbertson DT, Wang C. Cancer after kidney transplantation in the United States. *Am J Transplant*. 2004;4(6):905-913.
33. Wong G, Chapman JR, Craig JC. Cancer screening in renal transplant recipients: what is the evidence? *Clin J Am Soc Nephrol*. 2008;3(suppl 2):S87-S100.
34. U.S. Preventive Services Task Force. Recommendations for primary care practice. <http://www.uspreventiveservicestaskforce.org/Page/Name/recommendations>. Accessed October 31, 2014.
35. American Cancer Society. American Cancer Society guidelines for the early detection of cancer. <http://www.cancer.org/healthy/findcancerearly/cancerscreeningguidelines/american-cancer-society-guidelines-for-the-early-detection-of-cancer>. Accessed October 31, 2014.
36. Zwald FO, Brown M. Skin cancer in solid organ transplant recipients: advances in therapy and management: part I. Epidemiology of skin cancer in solid organ transplant recipients. *J Am Acad Dermatol*. 2011;65(2):253-261.
37. National Comprehensive Cancer Network. NCCN guidelines: squamous cell skin cancer. http://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf [registration required]. Accessed October 31, 2014.