Chapter 2
Overview of Solid Organ Transplantation for Primary Care Providers

Diana Zhong and Christopher J. Wong

Introduction

Solid organ transplantation is increasing in prevalence. With each passing year, it becomes more likely that primary care providers will encounter patients who are recipients of a solid organ transplant.

In the United States, the number of solid organ transplantations has risen steadily over the past 20 years (Fig. 2.1), with 36,529 solid organ transplants performed in 2018 [1]. The greatest increases have been in liver and kidney transplants (Fig. 2.2). As the actuarial survival has also increased over this period of time, so too has the overall prevalence of living solid organ transplant recipients. It is estimated that as of 2017, there were approximately 220,000 kidney transplant recipients [2], 84,000 liver transplant recipients [3], 32,000 heart transplant recipients [4], and 14,000 lung transplant recipients [5] living in the United States. In total, the number of living solid organ transplant recipients could populate an entire mid-size US city.

Internationally, the World Health Organization estimated that a total of 135,860 solid organ transplants were performed in 2016—a number that has been increasing annually based on provisional data, including in the United States [6]. The majority of solid organ transplants worldwide occur in high-income countries, but transplantation is spreading to an increasing number of countries [7].

The demographics of organ transplantation continue to change. Age is no longer a contraindication to transplantation at many transplant centers; although practices vary by country and region, some countries are moving away from age-based criteria [8, 9]. Indeed, 21% of transplants in the United States in 2018 were received by recipients aged 65 and over [1]. Donor demographics are also changing: there is now expanded use of potentially higher risk, or "extended criteria" donors to help

D. Zhong · C. J. Wong (✉)
Department of Medicine, Division of General Internal Medicine, University of Washington, Seattle, WA, USA
e-mail: zhongd@uw.edu; cjwong@uw.edu

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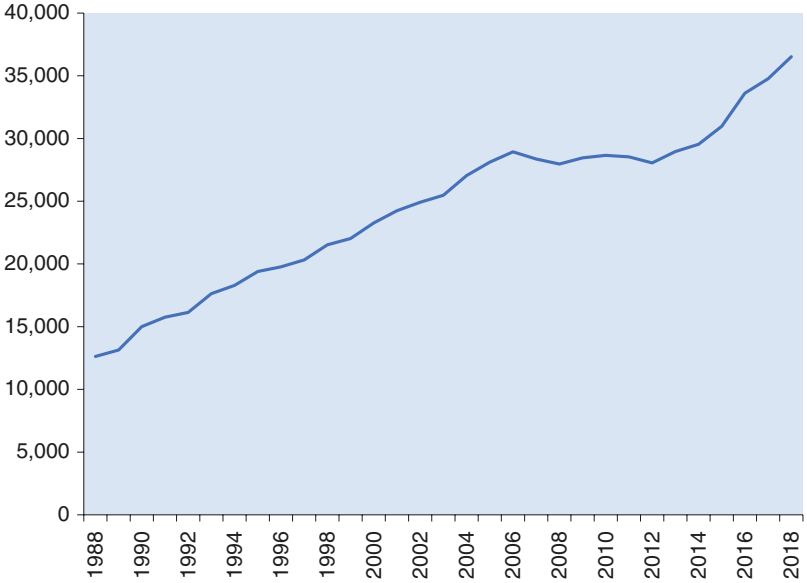

Fig. 2.1 Number of solid organ transplant recipients per year in the United States, 1988–2018. (Based on OPTN data from 2019, from https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/. Accessed April 22, 2019)

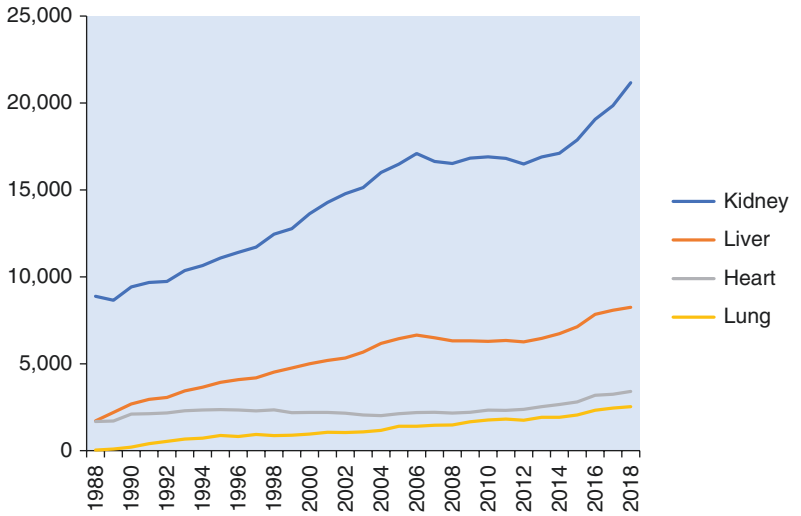

Fig. 2.2 Solid organ transplantation in the United States, by Organ, 1988–2018. *Kidney-pancreas, pancreas, heart-lung, and intestine transplantation data not shown. (Based on OPTN data from 2019, from https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/. Accessed April 22, 2019)

reduce the number of patients on the transplant waiting lists. Extended criteria vary, but may include older age donors as well as the presence of potentially treatable viruses such as hepatitis C [10]. Terminology varies, and some transplant specialists recommend using the least stigmatizing terms to classify donor organs so that providers are not dissuaded from recommending suitable donations.

There are many implications for primary care. First, the volume of solid organ transplant recipients will likely lead to more primary, urgent, and emergent medical care taking place outside of a transplant center. For example, there are an estimated 244 kidney transplant centers in the United States [11]. These centers would have to deliver primary care to all 220,000 living kidney transplant recipients while also evaluating the pre-transplant population; it is preferable that patients could continue routine care with their own primary care providers. Second, patients often live far from their transplant center, making it more imperative to have effective local care. In the United Kingdom, the median distance to the transplant center for liver transplant recipients was 67 km [12]. A study of patients in the United States' Veterans Affairs healthcare system found that distance from the transplant center was inversely correlated with being waitlisted for transplantation—notably in that same study, the vast majority of pre-liver transplant candidates were over 100 miles from a transplant center [13]. In another study of patients in the United States listed for liver transplant, 28% lived over 100 miles from the transplant center [14]. While it is conceivable that some solid organ transplant recipients may move closer to a transplant center after transplantation, this percentage is likely to be small. Third, lessening age requirements and improved overall survival are resulting in an increasingly older population of solid organ transplant recipients. The general practitioner, experienced in the comorbidities of aging, is well-suited to provide care for these patients.

Pre-Transplant Evaluation

Overview

While this book focuses on the primary care of patients after receiving a solid organ transplant, knowledge of the pre-transplant process is useful in their ongoing treatment.

The pre-transplant process begins when a patient with end-stage organ failure is referred to a transplant specialist. This referral may arise from primary care, a specialist, or during an acute-care hospitalization. Pre-transplant testing can take place in a variety of settings, including outpatient clinics (not necessarily only in the transplant center) and inpatient hospital stays.

The transplant team typically includes a medical and surgical team (for example, a transplant hepatologist and a transplant surgeon, in the case of end-stage liver disease), as well as a social worker and other staff to assess social support and

psychological health. Other specialists may be involved, such as an infectious disease specialist, psychiatrist, dietician, cardiologist, or pulmonologist, depending on the patient's needs and comorbidities. Testing generally includes laboratory studies, assessment of cardiac tolerance for surgery (other than for heart transplant), and cancer screening. Treatment often includes vaccinations and medication adjustments for medical optimization.

From there, a transplant committee evaluates a patient's candidacy for transplantation. The evaluation will include many factors, including the need for transplant, medical comorbidities, results of medical testing, suitability for major surgery, psychiatric evaluation, and other psychosocial considerations. If a patient is accepted as a candidate for transplantation, the patient is most commonly placed on a waiting list.

The transplant workup, evaluation, and candidate selection process vary depending on the transplant center, organ(s) affected, the patient's underlying disease, the urgency of transplantation, and many other individual patient factors. The information provided here is not intended to be comprehensive; rather, it will hopefully provide the primary care provider an overview of what the solid organ transplant recipient who presents to the outpatient clinic may have experienced prior to transplantation.

The pre-transplant evaluation is summarized in Table 2.1.

History and Exam

The initial pre-transplant medical evaluation will include a detailed history and physical exam. Active or chronic medical conditions are treated or optimized prior to transplantation. Severe medical conditions may be contraindications to transplantation, including untreatable significant dysfunction of another major organ system

Table 2.1 Pre-transplant evaluation

History and exam
Laboratory testing
Functional status
Nutrition and body mass index
Bone density
Cardiopulmonary assessment
Dental evaluation
Family planning (if applicable)
Infection screening
Immunizations
Cancer screening
Surgical evaluation
Psychosocial evaluation

(unless combined organ transplantation can be performed), uncorrected atherosclerotic disease with end-organ ischemia or coronary disease not amenable to revascularization, and other severe and uncorrectable diseases that may lead to a significantly shortened life expectancy [15, 16].

Laboratory Testing

Typical laboratory testing is shown in Table 2.2. In addition to routine testing, patients are evaluated for their risk of prior sensitization, including whether they have a history of blood or platelet transfusions, pregnancies, abortions, or previous transplants [15]. Patients are screened prior to transplant to help identify and treat active infections pre-transplant, to recognize infectious risks including latent infections, and to help prevent and manage post-transplant infections [17] (see "*Infections*" below).

Table 2.2 Typical pre-transplant laboratory tests

Routine tests [15, 18, 19]
Complete blood count
Kidney function and electrolytes
Liver function tests
Coagulation studies
Urinalysis and urine culture
Pregnancy test (if applicable)
Urine drug screen
Compatibility tests [15]
ABO-Rh blood type
Human leukocyte antigen (HLA) type
Panel reactive antibody assay (PRA)
Crossmatching
Infectious disease tests [17]
Human immunodeficiency virus (HIV): HIV antibody/antigen screening
Cytomegalovirus (CMV): CMV IgG
Hepatitis B virus (HBV): HBV surface antigen (HBsAg), HBV core antibody (HBcAb-IgM and IgG, or total core antibody), HBV surface antibody (HBsAb)
Hepatitis C virus (HCV): HCV antibody
HCV nucleic acid amplification testing (NAAT)
Epstein-Barr virus (EBV): EBV antibody (EBV viral capsid antigen IgG, IgM)
Toxoplasma gondii: *Toxoplasma* IgG antibody
Syphilis: available tests may vary by institution
Tuberculosis: Purified protein derivative (PPD) *or* Interferon gamma release assay (IGRA)
Additional testing if indicated by exposures and risk factors

Table 2.3 Pre-transplant cardiopulmonary screening tests

Most patients [21]:
Chest radiography (X-ray)
Electrocardiogram (ECG)
Depending on age and comorbidities, many patients will undergo further evaluation [21]:
Transthoracic echocardiogram (TTE)
Cardiac stress testing
Coronary angiography (if abnormal stress testing or echocardiogram)
Other testing considered may include [20]:
Cardiopulmonary exercise testing (CPET)
6-minute walk test (6MWT)
Noninvasive coronary CT angiography (CCTA)
Coronary artery calcium (CAC) score
Right heart catheterization
Some patients may have additional pulmonary evaluation with [18]:
Pulmonary function tests (PFTs)
Chest computed tomography (CT) scanning

Cardiopulmonary Screening

Screening is performed to evaluate for many cardiopulmonary conditions, including coronary artery disease, cardiomyopathy and heart failure, pulmonary hypertension, cardiac arrhythmias, valvular heart disease, and congenital heart disease [20]. Testing may vary by center, organ to be transplanted, and a patient's individual clinical features. Examples of cardiopulmonary testing are shown in Table 2.3.

Functional Status, Nutrition, and Bone Density

Poor functional status with limited rehabilitation potential may be a contraindication to transplantation. A patient's frailty can be assessed by whether they need assistance with activities of daily living (ADL), the sit-to-stand test, as well as whether they have unintentional weight loss and low physical activity [22]. Older age is increasingly not a contraindication by itself but is considered in the context of a patient's functional status and comorbidities [23].

Obesity can be a contraindication to transplantation. Patients are usually considered poor candidates for transplantation if they have a body mass index (BMI) $\geq$ 35 kg/m^2 for lung transplant candidacy and BMI $\geq$ 40 kg/m^2 for liver transplant candidacy. Conversely, malnourished patients are usually considered poor candidates as well [16, 18].

Most patients will have bone densitometry measured with dual-energy X-ray absorptiometry (DEXA). As patients will take chronic glucocorticoids

post-transplantation, having baseline data is helpful for follow-up testing and management [18].

Dental Evaluation

A dental evaluation is performed to evaluate for dental abscesses, dental caries, buried roots, and gum disease. Dental problems can be a source of post-transplant infection. Dental procedures are performed prior to transplantation whenever possible [18].

Family Planning

Pregnancy in the first 12 months following transplantation is associated with both an increased risk of preterm delivery as well as graft dysfunction or rejection. It is therefore recommended to avoid pregnancy in the first year after transplantation [24]. A patient's family planning goals should be addressed prior to transplantation, including contraception. Intrauterine devices (IUD) are a preferred and effective method of contraception that will avoid interactions with medications—if placed prior to transplantation, identifying the type of IUD and date of implantation is needed for future management.

Organ-Specific Testing

Further organ-specific testing is performed in conjunction with specialist consultation. While all such testing is not necessary to review, especially if no longer relevant (e.g., the organ is removed), some tests may be helpful for future management. For example, a patient with end-stage liver disease will likely have had esophagogastroduodenoscopy (EGD) performed to evaluate for esophageal varices—having the results of these evaluations may be useful for comparison if a repeat EGD is needed. Sometimes the workup for organ failure may uncover other syndromes that should be followed. For example, a monoclonal gammopathy may be identified during workup for chronic kidney disease; even if it was not the underlying etiology for the patient's kidney disease, it will still need to be followed post-transplantation. Finally, the explanted organ pathology may sometimes be useful. For example, a heart transplant recipient may have had negative biopsies, but on explant the finding of non-caseating granulomas may suggest sarcoidosis, a condition which could arise in other organs after transplantation.

Vaccines and Pre-transplant Prophylaxis

In most cases, the transplant team will attempt to make sure patients are as up to date as possible on vaccines *prior* to transplant [25]. Both inactivated and live-attenuated vaccines can be given to patients pre-transplant (unless otherwise contraindicated), but live vaccines are contraindicated post-transplant due to risk of disseminated infection. Additionally, vaccines have variable immunogenicity after transplant due to immunosuppression and thus may be less effective. Therefore, the pre-transplant window is a crucial time for most vaccines to be administered, ideally earlier in a patient's disease course as immunogenicity can also decline due to the relative immunocompromise from organ failure. It is recommended that live vaccines be administered by ≥4 weeks prior to immunosuppression, and that inactivated vaccines be administered ≥2 weeks prior to immunosuppression [24, 26]. All vaccines that are appropriate for age, exposure history, and immune status should be administered prior to transplantation according to the Centers for Disease Control (CDC) guidelines. In addition to the usual vaccine schedule, there are further recommendations for patients awaiting solid organ transplantation, which include hepatitis A, herpes zoster, and pneumococcal vaccination, as shown in Table 2.4 [25]. If a patient is unable to receive vaccinations prior to transplantation, an infectious disease specialist will typically assist with post-transplant vaccination decisions. (For post-transplant guidelines, see Chap. 12).

Less common vaccines that may have been given prior to transplant include meningococcus, Bacille Galmette-Guerin (BCG), smallpox, anthrax, rabies, yellow

Table 2.4 Typical vaccination recommendations prior to solid organ transplantation[a]

Vaccine	Type	Evaluate for serologic response?	Notes
Influenza inactivated (IIV)	Inactivated	No	High-dose formulation often used
Influenza live-attenuated (LAIV)	Live-attenuated	No	Intranasal vaccine*
Hepatitis B	Inactivated	Yes	Various formulations (2-dose, 3-dose, or 4-dose series)
Hepatitis A	Inactivated	Sometimes	Sometimes given in combined formulation with Hepatitis B vaccine
Tetanus	Inactivated	No	
Pertussis (Tdap)	Inactivated	No	If no tetanus booster in the past 10 years, administer Tdap. At least one dose of acellular pertussis should be given in adulthood, especially women of child-bearing age and individuals in contact with infants.
Inactivated Polio	Inactivated	No	
H. influenzae type B	Inactivated	Yes	

Table 2.4 (continued)

Vaccine	Type	Evaluate for serologic response?	Notes
S. pneumoniae	Inactivated	No	There are two inactivated vaccines, PCV13 (Prevnar 13®) and PPSV23 (Pneumovax 23®). See CDC guidelines for details, as timing and dosing vary based on indication. Most solid organ transplant recipients should have received at last PPSV23 prior to transplant, as it is indicated for patients with chronic lung disease, chronic liver disease, and chronic heart disease. Some patients will have also received PCV13 as it is indicated for patients with chronic renal failure, or if they were immunosuppressed pre-transplant for other medical conditions [27]. PCV13 should be completed 8 weeks prior to PPSV23 [24]
Human papilloma virus (HPV)	Inactivated	No	Indicated for age 9–45 years
Measles, mumps, rubella (MMR)	Live-attenuated	Yes	
Varicella (VAR or Varivax®)	Live-attenuated	Yes	Given if not immune
Herpes zoster (recombinant zoster vaccine, RZV or Shringrix®)	Inactivated	No	Recommended for patients ≥50 years old. This is generally the preferred form of zoster vaccination due to its higher efficacy as compared with the live-attenuated vaccine, and because it is inactivated it will not delay transplantation
Herpes zoster (live zoster vaccine, LZV or Zostavax®)	Live-attenuated	No	Two doses should be administered ≥3 months apart, while considering that live vaccines should be given ≥4 weeks prior to transplant [24]

[a]Recommendations change and should be reassessed periodically. All live vaccines are only administered if the patient is not already severely immunocompromised
*The intranasal, live-attenuated influenza vaccine is not recommended for adults age 50 and over; guidelines for this vaccine have changed periodically

fever, Japanese encephalitis, typhoid, and cholera, depending on a patient's exposures and travel [25].

Infections

Transplant candidates are assessed for past infections and a detailed exposure history (travel, residence, occupation, lifestyle, animal, and environmental) [17]. In addition to the routine laboratory testing shown in Table 2.2, further testing may be performed for patients with certain exposures or from endemic areas, including

assessment for *Strongyloides*, *Trypanosma cruzi*, and *Coccidioides* species [17, 28]. A rigorous separate screening process is used for potential organ donors.

HIV infection does not preclude receiving transplantation, though HIV should be well-controlled prior to pursuing transplantation [29]. Patients with hepatitis B and chronic hepatitis C can still be considered for transplantation but are evaluated for liver cirrhosis and considered for antiviral treatment prior to transplant [16, 23].

Viral serologies such as CMV and EBV testing can be used to guide donor selection and to stratify risk. Transplant recipients who are CMV seronegative are at higher risk for CMV infection if the donor is CMV seropositive; similarly, recipients who are EBV seronegative are at higher risk for EBV infection and post-transplant lymphoproliferative disorder (PTLD) if the donor is EBV seropositive. These cases require additional post-transplant monitoring and prevention strategies (see Chaps. 8 and 10) [17].

Colonization, Latent Infection, Chronic or Recurrent Infection, and Active Infection

Identification of infection risks can affect transplant candidacy and post-transplant treatment:

- *Colonization*: Microbial colonization can increase the risk of infection after transplantation. For example, a patient with cystic fibrosis awaiting lung transplantation may be colonized with multi-drug resistant strains of bacteria such as *Pseudomonas*, *Staphylococcus aureus, Stenotrophomonas*, and *Burkholderia*, as well as fungi such as *Aspergillus*. Patients are carefully evaluated to exclude active infection. Colonization with certain multi-drug resistant organisms or virulent organisms such as *Burkholderia* is associated with poor outcomes after transplantation and may be weighed as a consideration against transplantation [16]. Knowledge of this colonizing flora can aid in development of an individualized peri-transplant and post-transplant prophylactic antimicrobial regimen.
- *Latent infection*: Risk of recurrent infection is assessed and mitigated prior to transplantation. For example, a pre-transplantation history of active disease or seropositivity for coccidioidomycosis may warrant lifelong azole prophylaxis. In contrast, other endemic mycoses such as histoplasmosis are not routinely checked and do not directly alter management, but should be considered when evaluating a patient presenting with illness post-transplantation [17]. Patients with latent tuberculosis infection (LTBI) are ideally treated prior to transplantation [30].
- *Chronic or recurrent infections*: These infections generally require definitive treatment prior to transplantation. For example, patients with a history of severe and/or recurrent infection with *Clostridioides difficile* may receive secondary prevention with fecal microbiota transplant (FMT) or bezlotoxumab [31].
- *Active or uncontrolled infections*: These infections require treatment and often delay transplantation until the infection resolves or is controlled [17].

Cancer Screening

Pre-transplant evaluation requires age-appropriate cancer screening to be up to date. Patients with an active malignancy or recent history of malignancy will not be offered transplantation, as transplantation may not improve survival. Furthermore, immunosuppression increases the risk of malignancy post-transplant [32]. If a patient's cancer has been treated and the patient has been disease-free for a certain period of time, they may often be evaluated for transplantation [16, 19]. All patients should remain up to date on gender and age-appropriate cancer screening, which may include colonoscopy, mammogram, Papanicolaou (Pap) smear, skin examination, and additional screening if indicated for the patient's medical history (e.g., hepatocellular carcinoma screening for patients who have hepatitis B infection) [15].

Surgical Evaluation

A patient's surgical candidacy is a major component of the transplant evaluation, and factors in medical comorbidities as well as the patient's functional and nutritional status, as discussed above.

There are specific additional surgical considerations related to a patient's individual anatomy and history of prior surgeries and prior thromboses. Further workup such as CT scans or vascular studies may be warranted. Furthermore, depending on the organ site, there can be discussion of donor options (deceased, living, extended criteria donors). Specific comorbidities that confer especially high operative risk, such as portopulmonary hypertension in a patient with cirrhosis, will warrant evaluation with anesthesia and consultation with specialists [18]. A full discussion of the surgical evaluation is beyond the scope of this book.

Psychosocial Evaluation

The process of transplantation is fraught with difficult decisions and ethical dilemmas. Organs are a scarce resource. Although transplantation may be life-saving, patients are also encumbered by a lifelong need for medications, follow-up appointments, and management of care. Due to the immense post-transplant burden, the screening process for transplant candidacy encompasses many psychosocial factors, including having adequate social support, financial resources, and sufficient health literacy to be able to manage care. Unfortunately, these factors are often reflective of socioeconomic disparities [33].

Patients will be evaluated by a transplant social worker and often a transplant psychiatrist. There is not a universal evaluation metric, though several scoring scales exist [34, 35].

Patients will typically be evaluated for [34]:

- Treatment adherence and health behaviors
- Mental health history
- Substance use history
- Cognitive status and capacity to give informed consent
- Knowledge and understanding of their current illness
- Knowledge and understanding of current treatment options
- Coping abilities
- Social support
- Social history

Financial Evaluation

Depending on the country's health care system, the patient's insurance and the transplant center, financial approval may need to be secured at the beginning of the process to begin the transplant workup. In the United States, insurance coverage will be considered in terms of the costs of transplantation and post-transplantation care (including medication coverage), and the transplant center will typically have staff to assist with financial planning.

Psychiatric Evaluation

Patients with psychiatric disorders are required to have their diseases well-controlled prior to transplantation [16, 18]. Patients who are already taking psychotropic medications may need to have medications stopped or dose-reduced once transplant immunosuppression is introduced. For example, patients with bipolar disorder are often switched off of lithium to avoid postoperative metabolic shifts or renal insufficiency that could lead to medication toxicity. Such decisions should be made in conjunction with a transplant psychiatrist and a transplant pharmacist [36].

Depression and anxiety are common post-transplantation, either de novo or recurrent—knowing the patient's pre-transplant psychiatric history can be helpful with management after transplantation. Post-transplant patients have an increased risk of suicide and should be assessed regularly for mood disorders [37] (see Chap. 12).

Medication Adherence

Medication adherence is an important aspect of the psychosocial assessment. It is considered a contraindication to transplantation if a patient has current or a repeated history of medication non-adherence. Although a patient who has received a solid

organ transplant will have passed adherence screening prior to transplant, data suggest that adherence may be an ongoing concern after transplantation. Rates of post-transplantation medication nonadherence have been reported to be up to 36% in kidney transplant recipients and 7–15% in other transplant types [38]. Younger patients may be at higher risk for medication nonadherence: Kidney transplant recipients who are older adolescents and young adults (aged 17–24 years) have the highest risk of graft failure irrespective of transplant age; this is felt in part to be related to higher rates of immunosuppressive therapy nonadherence [39].

Substance Use

Ongoing substance abuse or dependence is a contraindication to transplantation. Evaluation for transplant often includes screening tests for nicotine use, alcohol, and recreational drugs. Illness related to substance use may be the primary reason that a patient requires transplantation, such as alcoholic cirrhosis, or chronic obstructive pulmonary disease due to smoking. If a patient is able to be treated for substance use pre-transplant and has good prognostic factors, they may then be reassessed for transplant candidacy [16].

- Tobacco: Smoking is a contraindication to lung transplantation. For other organ transplantation, smoking cessation is strongly preferred as smoking is associated with worse outcomes post-transplantation including increased risk of graft loss, cardiovascular events, and malignancy [40].
- Alcohol: Patients with alcoholic cirrhosis who have ceased alcohol use (typically 6 months, but may vary by transplant center) may be assessed for liver transplantation. However, sobriety for a certain time period is often not sufficient, as a pattern of use and subsequent return to use may portend a high risk of returning to use after transplantation; rather, patients with serious alcohol use disorders are referred to formal alcohol treatment programs [18].
- Marijuana: Institutions have varying policies regarding marijuana, but in most cases usage is unfavorable [16, 41].
- Opioid use disorder: Patients who have a well-controlled opioid-use disorder treated with methadone may still be considered for solid organ transplantation, and it is not required for transplant listing that methadone doses be reduced or discontinued [18]. Treatment with buprenorphine-naloxone for opioid use disorder is not a contraindication, but a transplant pharmacist should be consulted for perioperative and postoperative management.

Transplantation

Patients who successfully complete the pre-transplant evaluation and are approved by the transplant committee are then placed on a waiting list, unless the case is considered emergent. The waiting process can be among the most difficult and stressful

parts of the pre-transplant process. Despite yearly growth in the number of successful transplants performed, still more patients remain on the waiting list: in August 2019, over 124,000 individuals in the United States remained on the waiting list for an organ, over 3 times as many as were transplanted the year before [42]. Mortality while awaiting a transplant is significant; an estimated 20% of patients on the lung transplant waiting list will become too sick to transplant or die while on the waiting list [43, 44]. In addition to the numerical odds, the waiting process can be long and marked by worsening medical complications.

In some cases, patients are called for organ transplantation but do not receive an organ due to poor viability of the donated organ or other reasons—some patients have experienced several false alarms prior to transplantation.

Organ allocation and the initial transplant hospitalization are beyond the scope of primary care and are not covered in this book. Some patients have an uneventful course while others may have a difficult initial hospitalization. Early complications can include acute rejection, problems with the vascular or other anastomoses, thrombosis, and infection.

Returning to Primary Care

Patients who make it through the initial post-transplant hospitalization are usually discharged with prophylaxis against infections (see Chap. 8) and typically have a high dose of immunosuppression. In most cases, during the initial post-transplant period, patients will be cared for primarily by the transplant team.

After a period of time, the stable patient may "graduate" from the transplant program and be cared for by a community specialist along with a primary care provider. For example, a liver transplant recipient might return to primary care after 6 months and also be routinely followed by his or her local gastroenterologist; the patient may still return yearly to the transplant center (and more often if complications arise). The transition to primary care and local specialty care varies by transplant center, the patient's unique needs and preferences, and proximity to the transplant center.

Taking a Transplant History

When a solid organ transplant recipient enters (or re-enters) primary care, basic information should be obtained to optimize future care. The following data should be gathered (see Table 2.5) [45]:

Table 2.5 History-taking for the solid organ transplant recipient

History element	*Example*	Notes
Transplanted organ Indication Pre-transplant course	*Lung transplant, bilateral* *For cystic fibrosis, diagnosed at age 5* *Prior to transplant, had repeat exacerbations* *Also has non-pulmonary complications of cystic fibrosis (sinusitis, history of intestinal obstruction)*	Pre-transplant course varies widely. For renal transplant recipients, helpful to know if prior history of dialysis and type of dialysis access
Time course	*Date of transplant (month/year)*	The time since transplantation may affect target drug levels and risk of infection and malignancy
Graft function	*Spirometry (date) FEV1, FVC.* *Last bronchoscopy, if performed (date) (results)*	Assessment will vary depending on the transplanted organ
Complications Surgery-related Infections Rejection episodes (acute or chronic)	*Bronchial stenosis, status post airway dilation × 2* *Pneumonia in (month/year), bronchoscopy negative for rejection, fungal or viral infections; treated as community-acquired pneumonia* *No episodes of rejection*	If episodes of rejection, review treatment and doses (e.g., glucocorticoids, or increase in other immunosuppression)
Medications	*Tacrolimus 2 mg twice daily* *Mycophenolate mofetil 500 mg twice daily* *Prednisone 5 mg once daily*	See Chap. 3 If known, goal trough levels helpful to document
Serologic status Epstein-Barr Virus (EBV) Cytomegalovirus (CMV)	*EBV D+/R−* *CMV D+/R+*	D = Donor, R = Recipient The highest risk for EBV-related complications is in donor positive/recipient negative patients CMV prophylaxis is often given in the initial post-transplant period, depending on serostatus of the donor and recipient, as well as the induction immunosuppression used. See Chap. 8
Metabolic complications	*Hypertension* *Hypomagnesemia* *Chronic kidney disease stage 3* *Osteopenia: T-score −2.1, no history of facture*	See Chap. 11

Transplanted Organ

- Clearly listing the transplanted organ(s) and indication is helpful. Note that lung transplants can be single or bilateral. For kidney transplants, it is useful to document where the graft is located (usually in the lower pelvis—list which side). When applicable, the type of donor should be listed (kidney transplant recipients may have a living or cadaveric donor).
- Knowing the disease that led to organ transplantation is important, as it may recur in the graft. Examples include hepatitis C or autoimmune hepatitis that can develop again in the transplanted liver.
- A systemic condition or risk factor that led to organ transplantation may continue to affect other organ systems. Smoking may lead to chronic obstructive pulmonary disease and subsequent lung transplantation, but it may also be a risk factor for other cancers in the future. Cystic fibrosis may lead to lung transplantation, but its effects on the liver and gastrointestinal tract may continue. Alcohol use may recur in the liver transplant recipient, but even prior use may still be a risk factor for subsequent cancers.
- The pre-transplant course is often useful to review. Renal transplant recipients who have received hemodialysis may still have a fistula for access. Liver transplant recipients may have had recurrent gastrointestinal bleeding or encephalopathy, important considerations should graft failure occur.

Time Course

- As is discussed in Chap. 8, the time course after transplantation affects the general likelihood of opportunistic infections.
- Early infections (within the first month post-transplantation) are likely to be nosocomial or donor-derived, and are not typically encountered in primary care, as the patient will often primarily be in the care of the transplant team.
- In the 1–6 month time period, opportunistic infections can occur because of the higher levels of immunosuppression. Patients are usually still receiving the bulk of their care from the transplant team.
- After 6 months, community-acquired infections are common although some opportunistic infections still occur. For patients who experience a relatively uncomplicated post-transplantation course, many can transition the majority of their routine care to primary care around this time.
- If there is an episode of rejection that necessitates a higher level of immunosuppression, the time course is effectively "reset," with opportunistic infections becoming more likely.

Graft Function

- At primary care visits, providers should ask about symptoms of organ dysfunction.
- Surveillance studies of graft function should be reviewed. These tests are expected to be performed by the patient's specialist (typically either at the transplant center or by the local specialist). Function may be assessed by laboratory studies (creatinine in renal transplant recipients, hepatic function tests in liver transplant recipients), functional testing (spirometry in lung transplant recipients, echocardiograms in heart transplant recipients). Further testing varies by organ, transplant center, and individual patient, and may include imaging, biopsies, and immunosuppression levels.
- For more details, see organ-specific chapters (Chaps. 4, 5, 6, and 7).

Complications

- Surgery-related complications may include arterial or venous thrombosis, problems with vascular or other anastomoses, hernias, and surgical site infections. Organ-specific complications may occur. For example, hepatic artery thrombosis may occur early in liver transplantation; cardiac allograft vasculopathy is a unique form of coronary disease in the heart transplant recipient; lung transplantation can be complicated by airway stenoses requiring dilation.
- Opportunistic infections should be reviewed, including what organism, how the infection was confirmed, and what treatment was administered.
- Organ rejection should be asked about but also reviewed carefully in the medical record, as the presentation can vary widely. Sometimes organ rejection is asymptomatic and found on routine biopsy—therefore, patients may only be superficially aware of it.
- For more details, see organ-specific chapters (Chaps. 4, 5, 6, and 7).

Medications

- A thorough medication history should be taken, including supplements and non-transplant medications, as drug interactions are common. If patients see other providers who prescribe medications, those records should be obtained and reviewed.

- Adherence should be investigated. With good pre- and post-transplant education, patients are doubtless aware of the implications of having a transplanted organ and the importance of strict adherence to immunosuppressive medications. Nevertheless, many patients feel burdened not only by their transplantation and fear of graft rejection, but also by their medications, with concern for cancers and infections as a risk of their immunosuppression [46]. There is a significant post-transplant financial and emotional burden from medications, medical appointments, and hospitalizations [35, 46].
- Side effects should be addressed, both to help assess a patient's tolerance of their medications, but also as a factor potentially affecting adherence. Familiarity with common side effects of anti-rejection medications will facilitate history-taking about symptoms.
- Depending on the immunosuppression medication, the transplant specialist will be following medication levels. These are typically trough levels (i.e., immediately before the next dose). It is helpful to document the goal trough level if it is known.
- Anti-rejection medications are reviewed in Chap. 3.

Serologic Status

- Obtaining and documenting the EBV and CMV data for the recipient and the donor is useful, as it may affect viral prophylaxis (which will typically be managed by the transplant specialist) but also the risk of future infection or malignancy (See Chaps. 8 and 10).

Metabolic Complications

- Ask about and review the patient's chart for metabolic complications and comorbidities, including electrolyte imbalances, diabetes, hypertension, osteoporosis, and history of cancer (See Chap. 11).

Examination

- General physical examination should be performed as with non-transplant patients.
- Examine the surgical incision for signs of infection or hernia.
- Examine the transplanted organ system for signs of dysfunction.
  - The heart transplant recipient should have a thorough cardiopulmonary exam evaluating for signs of heart failure. The transplanted heart is denervated and

patients may not have classic angina if coronary artery disease occurs. Tachycardia may be a sign of rejection.
- The lung transplant recipient may have received a single or double lung transplant. Single lung transplant recipients may still have serious disease in the native lung. In the transplanted lung, rales or dyspnea may signal infection or rejection, but often rejection can be subtle without prominent exam findings.
- The liver transplant recipient should be examined for signs of cirrhosis; otherwise, dysfunction may not present on exam but instead be detected on laboratory findings. Splenomegaly may persist after transplantation.
- The kidney transplant recipient will typically have the transplanted kidney seated in the lower pelvis, often palpable on exam. The abdominal exam should be conducted with care—while one should look for signs of inflammation, one should not apply excessive pressure on the transplanted kidney itself.
- For more details, see Chaps. 4, 5, 6, and 7.

Establishing a Follow-Up Plan

- Patients who are doing very well—e.g., with a well-functioning graft, good adherence, and no history of graft rejection or opportunistic infections—might only need to see primary care and the transplant clinic yearly, with more frequent laboratory monitoring in between.
- Other patients who are at higher risk may continue quarterly visits, or even more frequently.
- Practice varies by transplant center and organ transplanted.
- Establish preventive health recommendations. Future metabolic testing should be assessed and coordinated with the transplant team. A plan for future immunizations should be made, and patients should be reminded that they can no longer receive live vaccines. For additional discussion, see Chap. 12.

Pearls

- *Inquire about the pre-transplant process.* Many patients will be forward-thinking and not wish to relive the pre-transplant process. However, if the primary care provider did not care for the patient pre-transplant, it can be useful to explore the pre-transplant course from the patient's perspective. For many patients, their life prior to transplantation is marked by years of chronic illness. The process of transplant evaluation can be a lengthy and harrowing one for many patients, and the subsequent wait for transplantation is yet another ordeal. Some patients have to travel great distances from their home. As organs are a scarce resource, the waiting process can be emotionally and psychologically difficult. Some patients have experienced healthcare-related trauma from intensive-care unit or other hospital stays.

Conversely, a smaller proportion of patients may have had a brief severe illness prior to transplantation. For example, a previously healthy patient presenting with acute fulminant liver failure may not have had the physical and psychological sequelae of chronic illness, or may have had limited primary care contact prior to transplantation.

- *Recordkeeping*. Gathering the pre-transplant and post-transplant information for a solid organ transplant recipient can be challenging, depending on the medical record system, whether the primary care provider and transplant specialists practice in the same healthcare system, and the culture of communication between providers. Ideally, the transplant team has summarized the pre-transplant evaluation in their documentation, with similarly detailed post-transplant surveillance in the medical record. However, obtaining additional records is sometimes required. These baseline tests can be very helpful as a basis of comparison if complications arise.
- *Communicate and consult early*. While one goal of this book is to improve the primary care provider's familiarity with the care of solid organ transplant recipients, even with the most meticulous care, the health of a solid organ transplant recipient can decline rapidly. If there is concern for graft dysfunction or an opportunistic infection, the primary care provider should consult with the transplant specialist. Many specialty centers have medical specialists who have additional expertise in transplant medicine (e.g., a transplant infectious disease specialist or a transplant pharmacist). It is recommended to review the expertise in one's local practice area, as well as the preferred consultants of the patient's transplant team. If there is uncertainty about an aspect of a patient's care, it is best to err on the side of communicating with the transplant team. Most transplant centers have a robust multidisciplinary team to help communicate and coordinate care.

Conclusion

Primary care providers have an increasingly vital role in the outpatient care of solid organ transplant recipients. While care of such patients can be complex, the ability to review a patient's prior transplant evaluations and assess the patient's current health status prepares the primary care provider to optimize future preventive care and address acute medical concerns.

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