Current PSYCHIATRY

Tools, techniques to assess organ transplant candidates

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Address anxiety, depression, and substance abuse before and after surgery

With nearly 30,000 organ transplants being performed in the United States each year (*Box 1*),[1] demand is growing for psychiatrists to provide presurgical and ongoing care.

How you might collaborate with a transplant team depends on each medical center's protocols and individual patients' mental health needs. A transplant candidate with depressive or anxiety symptoms may be referred to you for presurgical stabilization, for example, particularly if the patient lives far from a highly specialized transplant center.

Transplant assessments differ from usual psychiatric evaluations. Your findings will be used to help the transplant team evaluate the patient's demographics, disease severity, and resources to give the patient the best chance for medical recovery. Inform patients at the beginning of the pretransplant evaluation that the results:

- will be shared with the transplant team
- may be used to help make decisions about transplant
- will not be the only factor determining if a transplant center will place a patient on an organ wait list.[2]

Pretransplant evaluation

Presurgical assessment helps determine the patient's understanding of the transplant process and ability to provide consent (*Table 1*).[3] Patients do not need a high level of medical sophistication to discuss transplantation, but they must understand the

Box 1

Organ transplants: Not experimental anymore

In 2006, U.S. surgeons performed 28,931 organ transplants, bringing the total number of transplants since 1988 to >400,000. Each year, more kidney transplants are performed (17,091 in 2006) than all other organ transplants combined, according to the nonprofit United Network of Organ Sharing.[1]

Other organs being transplanted include liver, pancreas, heart, lung, and intestine. Some patients receive multiple organs, such as kidney/pancreas or heart/lung. As this article went to press, >96,000 candidates were on wait lists for organ donations.

Survival after transplantation has improved because of better immunosuppressant therapies introduced in the early 1980s and evolving physician and institutional experience. One-year survival rates for single-organ transplants range from 85% for lung to 98% for living donor kidney. Five-year survival rates range from 47% for lung to 86% for living donor kidney.

Source: Reference 1

basics of the procedure and be able to rationally discuss their options. If a patient has severe cognitive impairment, dementia, or hepatic encephalopathy and cannot participate in the consent process, a surrogate is necessary.

Explore the patient's attitudes and beliefs about transplant. If other team members have educated the patient about the procedure, your assessment can help determine how much the patient understood and if the patient has the capacity to make treatment decisions. Some patients believe the operation will "cure" them, despite education about the rigorous posttransplant routine. Alert the transplant team to these views, and begin aligning the patient's views with reality.

Assessing psychiatric comorbidity. Like other patients with life-threatening medical illnesses, many transplant patients present with major depression and anxiety. Screen for symptoms of mood and anxiety disorders and past episodes of depression or mania. Explore the patient's response to psychiatric treatment, current therapies, and history of treatment adherence.

Depression. Patients listed for transplant are seriously ill and coping with the difficulties of the sick role. Organ failure symptoms and resultant disability—such as insomnia, anorexia, fatigue, and impaired concentration—overlap with depression's neurovegetative signs. Suspect depression if a patient presents with anhedonia, tearfulness, apathy, or guilt.

Among heart, lung, and liver transplant candidates, the reported lifetime prevalence of depression averages approximately 20%.[4-6]

Anxiety disorders. An estimated 40% of transplant patients have anxiety disorders,[7] which may be caused by:

- stress of chronic illness
- uncertainty of the transplant process
- medical conditions such as hypothyroidism or pulmonary embolism.

Chronic mental illness. Patients with major mental illnesses such as schizophrenia might be appropriate candidates for organ transplant if they have adequate social support and history of treatment compliance.

Table 1

Psychiatric assessment of the pretransplant patient

Assess understanding of his or her illness
Assess understanding of transplant process and ability to provide informed consent
Assess history of compliance with medical and psychiatric treatments
Identify substance abuse and other psychiatric comorbidities
Assess mental status
Evaluate social support system and possible interventions to bolster supports
Provide transplant team with information about patient's need for education and support
Recommend treatment plan to address substance abuse and other psychiatric comorbidities

Source: Adapted from reference 3

Pharmacotherapy. Because of the variety of medical problems seen in transplant candidates, carefully consider medication side effects and drug-drug interactions when prescribing psychotropics.

Antidepressants. Among the selective serotonin reuptake inhibitors (SSRIs), citalopram, escitalopram, and sertraline are least likely to affect hepatic metabolism of other medications (*Table 2, page 58*).[8] If a patient presents with liver failure, reduce the dosages of medications with hepatic metabolism.

Benzodiazepines. Use caution when treating anxiety with benzodiazepines because of the risk of tolerance, withdrawal, and dependence. Avoid benzodiazepines when treating transplant candidates with a substance abuse history. Also, these drugs might worsen hepatic encephalopathy and increase confusion.

Patients awaiting lung transplantation, especially those with high levels of CO_2 retention, require special care because benzodiazepines might decrease respiratory drive. Try other agents such as buspirone, gabapentin, SSRIs, or second-generation antipsychotics to treat their anxiety.

Psychotherapy. Supportive psychotherapy can help patients navigate the often-

Clinical Point

Organ failure symptoms and resultant disability overlap with depression's neurovegetative signs

Clinical Point

Effective treatment of substance abuse is essential because 30% to 50% of liver transplant patients relapse after the procedure

Table 2

Antidepressants' half-life and effect on hepatic metabolism

	Hepatic enzyme alterations	Half-life (hours)
SSRIs		
Fluoxetine	2D6, 2C9, 2C19, 3A4 inhibition	72
Citalopram	None	35
Escitalopram	2D6 inhibition (weak)	32
Sertraline	2D6 inhibition (weak)	30
Paroxetine	2D6 inhibition (strong)	18
Fluvoxamine	1A2, 2C19, 2C9, 3A4 inhibition	18
Others		
Mirtazapine	None	30
Bupropion SR	2D6 inhibition	21
Venlafaxine XR	2D6 inhibition	5
Trazodone	None	5

SSRIs: selective serotonin reuptake inhibitors
Source: Reference 8

lengthy process of waiting for a donor organ. Support groups for organ transplant candidates may help ease patients' depressive symptoms.

Assessing substance abuse

Up to 50% of liver transplant candidates have a history of alcohol and/or drug abuse,[9] the highest rate among transplant populations. Alcohol-induced cirrhosis and hepatitis C contracted from IV drug use are common indications for liver transplant. Effective treatment of substance abuse is essential because 30% to 50% of these patients relapse after the procedure.[10] Assess:

- each substance abused, including onset, peak, and current use
- family history of substance abuse disorders
- past efforts at rehabilitation
- tobacco use (smoking before and after transplant is related to an increased incidence of new cancer diagnoses).[11]

Some transplant centers require patients with substance use disorders to participate in 12-step programs or rehabilitation. Regardless of the institutions' requirements, encourage patients to participate in rehabilitation to prevent relapse and mitigate the negative impact of substance abuse on physical and mental well-being.

Mental status examination includes the usual elements such as appearance, behavior, speech, affect, and thought process. Assess for suicidal thinking or hopelessness, which have been linked to serious medical illness.[12] Question patients about hallucinations and give special attention to visual aberrations, which may occur in medically ill patients.

Cognitive testing. Use tools such as the Mini-Mental State Examination, clock drawing test, and Trail Making A and B tests to assess cognitive ability. If patients show signs of cognitive impairment, arrange for follow-up examinations and refer for neuropsychological testing.

Some cognitive impairment—such as that caused by hepatic encephalopathy—will likely improve after transplant, but other types—such as that caused by vascular disease—will not. If confusion is caused by hepatic encephalopathy, treatment with lactulose might rapidly improve symptoms. Remember that patients with hepatic encephalopathy might not exhibit elevated ammonia levels. Underlying causes of worsening hepatic encephalopathy—such as infections or bleeding—might require treatment.

Assessing adherence. Medication adherence after transplant is essential to prevent organ rejection and other complications. Posttransplant regimens are complex, and the frequency of follow-up assessments can be intense—particularly in the first year after transplant.

Your pretransplant assessment can identify where patients have struggled with adherence in the past. Before the transplant, your team can work to correct barriers such as inability to pay for medications, child care problems, or transportation needs.

Personality disorders have been identified as predictors of posttransplant

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highest dose of oral olanzapine (15±2.5 mg/d). In controlled clinical trials of intramuscular olanzapine for injection, there were no statistically significant differences from placebo in occurrence of any treatment-emergent extrapyramidal symptoms, assessed by either rating scales incidence or spontaneously reported adverse events.

Other Adverse Events: Dose-relatedness of adverse events was assessed using data from this same clinical trial involving 3 fixed oral dosage ranges (5±2.5, 10±2.5, or 15±2.5 mg/d) compared with placebo. The following treatment-emergent events showed a statistically significant trend: asthenia, dry mouth, nausea, somnolence, tremor.

In an 8-week, randomized, double-blind study in patients with schizophrenia, schizophreniform disorder, or schizoaffective disorder comparing fixed doses of 10, 20, and 40 mg/d, statistically significant differences were seen between doses for the following: baseline to endpoint weight gain, 10 vs 40 mg/d; incidence of treatment-emergent prolactin elevations >24.2 ng/mL (female) or >18.77 ng/mL (male), 10 vs 40 mg/d and 20 vs 40 mg/d; fatigue, 10 vs 40 mg/d and 20 vs 40 mg/d; and dizziness, 20 vs 40 mg/d.

Vital Sign Changes—Oral olanzapine was associated with orthostatic hypotension and tachycardia in clinical trials. Intramuscular olanzapine for injection was associated with bradycardia, hypotension, and tachycardia in clinical trials (*see* PRECAUTIONS).

Weight Gain—In placebo-controlled 6-week schizophrenia studies, weight gain was reported in 5.6% of oral olanzapine patients (average 2.8-kg gain) compared to 0.8% of placebo patients (average 0.4-kg loss); 29% of olanzapine patients gained >7% of their baseline weight, compared to 3% of placebo patients. During continuation therapy (238 median days of exposure), 56% of patients met the criterion for having gained >7% of their baseline weight. Average gain during long-term therapy was 5.4 kg.

Laboratory Changes—Olanzapine is associated with asymptomatic increases in SGPT, SGOT, and GGT and with increases in serum prolactin and CPK (*see* PRECAUTIONS). Asymptomatic elevation of eosinophils was reported in 0.3% of olanzapine patients in premarketing trials. There was no indication of a risk of clinically significant neutropenia associated with olanzapine in the premarketing database.

In clinical trials among olanzapine-treated patients with baseline random triglyceride levels of <150 mg/dL (N=659), 0.5% experienced triglyceride levels of ≥500 mg/dL anytime during the trials. In these same trials, olanzapine-treated patients (N=1185) had a mean triglyceride increase of 20 mg/dL from a mean baseline of 175 mg/dL. In placebo-controlled trials, olanzapine-treated patients with baseline random cholesterol levels of <200 mg/dL (N=1034) experienced cholesterol levels of ≥240 mg/dL anytime during the trials more often than placebo-treated patients (N=602; 3.6% vs 2.2% respectively). In these same trials, olanzapine-treated patients (N=2528) had a mean increase of 0.4 mg/dL in cholesterol from a mean baseline of 203 mg/dL, which was significantly different compared to placebo-treated patients (N=1415) with a mean decrease of 4.6 mg/dL from a mean baseline of 203 mg/dL.

ECG Changes—Analyses of pooled placebo-controlled trials revealed no statistically significant olanzapine/placebo differences in incidence of potentially important changes in ECG parameters, including QT, QTc, and PR intervals. Olanzapine was associated with a mean increase in heart rate of 2.4 BPM compared to no change among placebo patients.

Other Adverse Events Observed During Clinical Trials—The following treatment-emergent events were reported with oral olanzapine at multiple doses ≥1 mg/d in clinical trials (8661 patients, 4165 patient-years of exposure). This list may not include events previously listed elsewhere in labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening. *Frequent* events occurred in ≥1/100 patients; *infrequent* events occurred in 1/100 to 1/1000 patients; *rare* events occurred in <1/1000 patients. ***Body as a Whole***—*Frequent:* dental pain, flu syndrome; *Infrequent:* abdomen enlarged, chills, face edema, intentional injury, malaise, moniliasis, neck pain, neck rigidity, pelvic pain, photosensitivity reaction, suicide attempt; *Rare:* chills and fever, hangover effect, sudden death. ***Cardiovascular***—*Frequent:* hypotension; *Infrequent:* atrial fibrillation, bradycardia, cerebrovascular accident, congestive heart failure, heart arrest, hemorrhage, migraine, pallor, palpitation, vasodilatation, ventricular extrasystoles; *Rare:* arteritis, heart failure, pulmonary embolus. ***Digestive***—*Frequent:* flatulence, increased salivation, thirst; *Infrequent:* dysphagia, esophagitis, fecal impaction, fecal incontinence, gastritis, gastroenteritis, gingivitis, hepatitis, melena, mouth ulceration, nausea and vomiting, oral moniliasis, periodontal abscess, rectal hemorrhage, stomatitis, tongue edema, tooth caries; *Rare:* aphthous stomatitis, enteritis, eructation, esophageal ulcer, glossitis, ileus, intestinal obstruction, liver fatty deposit, tongue discoloration. ***Endocrine***—*Infrequent:* diabetes mellitus; *Rare:* diabetic acidosis, goiter. ***Hemic and Lymphatic***—*Infrequent:* anemia, cyanosis, leukocytosis, leukopenia, lymphadenopathy, thrombocytopenia; *Rare:* normocytic anemia, thrombocythemia. ***Metabolic and Nutritional***—*Infrequent:* acidosis, alkaline phosphatase increased, bilirubinemia, dehydration, hypercholesteremia, hyperglycemia, hyperlipemia, hyperuricemia, hypoglycemia, hypokalemia, hyponatremia, lower extremity edema, upper extremity edema; *Rare:* gout, hyperkalemia, hypernatremia, hypoproteinemia, ketosis, water intoxication. ***Musculoskeletal***—*Frequent:* joint stiffness, twitching; *Infrequent:* arthritis, arthrosis, leg cramps, myasthenia; *Rare:* bone pain, bursitis, myopathy, osteoporosis, rheumatoid arthritis. ***Nervous System***—*Frequent:* abnormal dreams, amnesia, delusions, emotional lability, euphoria, manic reaction, paresthesia, schizophrenic reaction; *Infrequent:* akinesia, alcohol misuse, antisocial reaction, ataxia, CNS stimulation, cogwheel rigidity, delirium, dementia, depersonalization, dysarthria, facial paralysis, hypesthesia, hypokinesia, hypotonia, incoordination, libido decreased, libido increased, obsessive compulsive symptoms, phobias, somatization, stimulant misuse, stupor, stuttering, tardive dyskinesia, vertigo, withdrawal syndrome; *Rare:* circumoral paresthesia, coma, encephalopathy, neuralgia, neuropathy, nystagmus, paralysis, subarachnoid hemorrhage, tobacco misuse. ***Respiratory***—*Frequent:* dyspnea; *Infrequent:* apnea, asthma, epistaxis, hemoptysis, hyperventilation, hypoxia, laryngitis, voice alteration; *Rare:* atelectasis, hiccup, hypoventilation, lung edema, stridor. ***Skin and Appendages***—*Frequent:* sweating; *Infrequent:* alopecia, contact dermatitis, dry skin, eczema, maculopapular rash, pruritus, seborrhea, skin discoloration, skin ulcer, urticaria, vesiculobullous rash; *Rare:* hirsutism, pustular rash. ***Special Senses***—*Frequent:* conjunctivitis; *Infrequent:* abnormality of accommodation, blepharitis, cataract, deafness, diplopia, dry eyes, ear pain, eye hemorrhage, eye inflammation, eye pain, ocular muscle abnormality, taste perversion, tinnitus; *Rare:* corneal lesion, glaucoma, keratoconjunctivitis, macular hypopigmentation, miosis, mydriasis, pigment deposits lens. ***Urogenital***—*Frequent:* vaginitis*; *Infrequent:* abnormal ejaculation,* amenorrhea,* breast pain, cystitis, decreased menstruation,* dysuria, female lactation,* glycosuria, gynecomastia, hematuria, impotence,* increased menstruation,* menorrhagia,* metrorrhagia,* polyuria, premenstrual syndrome,* pyuria, urinary frequency, urinary retention, urinary urgency, urination impaired, uterine fibroids enlarged,* vaginal hemorrhage*; *Rare:* albuminuria, breast enlargement, mastitis, oliguria. (*Adjusted for gender.)

The following treatment-emergent events were reported with intramuscular olanzapine for injection at one or more doses ≥2.5 mg/injection in clinical trials (722 patients). This list may not include events previously listed elsewhere in labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening. ***Body as a Whole***—*Frequent:* injection site pain; *Infrequent:* abdominal pain, fever. ***Cardiovascular***—*Infrequent:* AV block, heart block, syncope. ***Digestive***—*Infrequent:* diarrhea, nausea. ***Hemic and Lymphatic***—*Infrequent:* anemia. ***Metabolic and Nutritional***—*Infrequent:* creatine phosphokinase increased, dehydration, hyperkalemia. ***Musculoskeletal***—*Infrequent:* twitching. ***Nervous System***—*Infrequent:* abnormal gait, akathisia, articulation impairment, confusion, emotional lability. ***Skin and Appendages***—*Infrequent:* sweating.

Postintroduction Reports—Reported since market introduction and temporally (not necessarily causally) related to olanzapine therapy: allergic reaction (eg, anaphylactoid reaction, angioedema, pruritus or urticaria), diabetic coma, jaundice, neutropenia, pancreatitis, priapism, rhabdomyolysis, and venous thromboembolic events (including pulmonary embolism and deep venous thrombosis). Random cholesterol levels of ≥240 mg/dL and random triglyceride levels of ≥1000 mg/dL have been reported.

DRUG ABUSE AND DEPENDENCE: Olanzapine is not a controlled substance.

Literature revised November 30, 2006

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Box 2

What is 'adequate' social support?

When assessing a patient's social support, look for evidence of:

- stable living situations
- long-term relationships with spouses, parents, children, or close friends
- adequate financial resources, including health insurance.

These factors help the patient manage the posttransplant process and numerous follow-up physician visits. Religious organizations or other social institutions also appear to provide the emotional support patients need to cope with an organ transplant.

nonadherence, and 50% to 60% of transplant programs consider personality disorders a relative contraindication to organ transplant.[13] Address other contributors to poor adherence—such as substance abuse or depression—with ongoing psychiatric care.

Social support is essential to help with the normal difficulties such as frequent clinic visits and initial physical disability patients face after successful transplant (***Box 2***). Ask about the candidate's family, friends, spirituality, and finances during your pretransplant assessment. Poor social support is related to the development of posttransplant psychiatric disorders[14] and adherence difficulties.[15]

Assessment instruments—such as the Psychosocial Assessment of Candidates for Transplantation and the Transplant Evaluation Rating Scale[3]—include social support items and can be useful in identifying weak areas.

Data collected by other team members can be invaluable. A nurse or social worker, for example, may observe that a patient is unwilling to take medications, contrary to the patient's report. Other sources of information include the patient's family and friends, a primary care physician, or other mental health providers such as a therapist or case manager.

Posttransplant psychiatric care

Depression. The incidence of depression is higher in the year following transplant than before transplant or in the immediate posttransplant period.[5] Predictors of posttransplant depression include:

- history of depression
- poor social support

- passive coping strategies
- poor physical status after transplantation.[16,17]

Carefully monitor patients who present with these factors after transplant. Treat depression with supportive measures designed to improve the patient's social network and coping skills and pharmacotherapy. Select antidepressant medications based on side effect profiles and impact on the patient's transplanted organs.

Substance abuse. Patients with a pretransplant history of substance abuse often relapse. Among transplant recipients with a history of alcoholic liver disease, drinking rates of 30% to 40% have been reported 5 years after transplant. Most of these data represent occasional use, not heavy or regular drinking.[18] Relapse can occur despite careful assessment and follow-up.

Some evidence suggests that transplant patients who resume drinking have worse outcomes than those who abstain. Alcoholism relapse has other negative consequences, such as relationship problems and employment difficulties.

Predictors of relapse include:

- pretransplant history of alcohol dependence
- family history of alcoholism
- rehabilitation history, which could indicate a severe substance abuse disorder.[3]

Medications for alcoholism treatment have not been studied systematically in transplant patients, but low doses of acamprosate, ≤2 g/d, and naltrexone, ≤200 mg/d, are options for patients interested in pharmacotherapy. Support from 12-step programs also helps treat substance-abusing patients.

Altered mental status. Immunosuppressive medications—including cyclosporine, tacrolimus, and prednisone—can have neuropsychiatric effects and could cause a change in mental status (***Table 3***).[19] Check cyclosporine and tacrolimus serum levels against reference ranges when delirium is present. If levels are toxic the dosage often can be lowered, which might lead to clinical improvement.

Table 3

Neuropsychiatric side effects of medications commonly used in transplant patients

Medication	Side effects
Cyclosporine	Tremor, headache, seizures, hallucinations, delirium
Tacrolimus	Tremor, headache, vivid dreams, anxiety, anorexia, seizures, delirium
Prednisone	Depression, mania, psychosis, delirium

Source: Adapted from references 3,7

Quality of life. In general, patients' quality of life improves after their transplant. After the first year—which patients might find difficult because of changes in physical and social status—quality of life typically improves.[5]

Psychiatric disorders such as depression can worsen quality of life. However, quality of life can improve after depression is diagnosed and treated. Other predictors of improved quality of life include older age, marriage, and the absence of a personality disorder.[4]

Other posttransplant concerns of patients include changes in employment, finances, and relationships. Patients often have been away from work before transplant, and returning after a long absence can be stressful. Patients may find that they cannot work as well as before becoming ill, which may lead to frustration, depression, and/or anxiety symptoms. Transplant surgery requires a large financial investment, and money concerns usually persist long after the transplant.

The transplant recipient's role within the family may shift after surgery. Families might expect the patient to "return to normal" and resume old activities. Alternatively, family members might continue to treat the patient as a person with chronic illness despite physical improvement. If patients are struggling with these changes, supportive psychotherapy is indicated.

Clinical Point

The incidence of depression is higher in the year following transplant than before transplant or immediately posttransplant

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continued

Related Resources

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Drug Brand Names

Acamprosate • Campral
Buspirone • BuSpar
Bupropion SR • Wellbutrin SR
Citalopram • Celexa
Cyclosporine • Sandimmune
Escitalopram • Lexapro
Fluoxetine • Prozac
Fluvoxamine • Luvox
Gabapentin • Neurontin
Lactulose • Cephulac, Chronulac
Mirtazapine • Remeron
Naltrexone • ReVia
Paroxetine • Paxil
Prednisone • Deltasone
Sertraline • Zoloft
Tacrolimus • Prograf
Trazodone • Desyrel

Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

Clinical Point

Posttransplant patients might not be able to work as well as before becoming ill, leading to depression or anxiety

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Bottom Line

As survival rates and quality of life for organ transplant patients improve, the number of patients awaiting and receiving transplants will increase. The psychiatric management of these patients can improve quality of life and strengthen coping skills during difficult times. Managing depression and anxiety before and after transplant can increase the probability of a successful medical outcome for patients and their families.