Psychiatric aspects of organ transplantation

AUTHOR: John Vella, MD, FACP, FRCP, FASN, FAST
SECTION EDITOR: Jonathan M Silver, MD
DEPUTY EDITOR: David Solomon, MD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Oct 2023.**
This topic last updated: **Apr 15, 2023.**

INTRODUCTION

The development of end-stage organ failure combined with the realization that life may no longer be possible without medical intervention can lead to depression, anxiety, nonadherence with diet or medication, and sexual dysfunction in the transplant patient [1,2]. The administration of immunosuppressive drugs, such as glucocorticoids and calcineurin inhibitors, has also been implicated in causing psychiatric disturbances [3,4]; these include euphoria, delirium, generalized anxiety disorder, and hallucinosis.

These disorders frequently require treatment with psychopharmacologic agents. However, their administration may be hazardous because of adverse effects as well as specific interactions with immunosuppressive drugs.

This topic review will discuss some of the more common psychiatric disturbances that develop in transplant recipients with specific attention to their impact upon pharmacologic management and prognosis. Discussions related to psychotherapy are presented separately.

PSYCHOLOGICAL IMPACT OF TRANSPLANTATION

The altruistic act of kidney donation appears to confer psychologic benefit to the donor. In a study of donors followed after a period of 5 to 10 years, the majority of individuals, independent of the outcome of the procedure, expressed positive feelings towards having donated a kidney [3]. However, in another survey, donating was perceived to have had a negative impact upon

the health and finances of 15 and 23 percent of responding donors, respectively [4]. Despite this perception, donors of kidneys live longer than others, due most probably to the screening process, which only permits healthy persons to be accepted for living kidney donation [5].

For the graft recipient, transplantation means more than an operation; it requires a certain degree of personal strength and adequate coping skills. In a study of heart transplant recipients, patients were grouped according to their response to a psychological survey [6]:

- Patients in group 1 denied thinking about the donor.
- Patients in group 2 were partial deniers who were aware that they avoided thinking about the donor.
- Patients in group 3 accepted the death of the donor as reality and also reported having more or less close connections with the donor.

Eighty two percent of the patients interviewed accepted the donor heart immediately as their own, whereas the remaining 18 percent avoided talking and thinking about the graft and donor. Thus, transplant recipients use different defense mechanisms concerning their transplanted organ to help them cope with their medical condition.

Kidney recipients also have particular difficulty asking and/or involving a possible living donor. Patients do not pursue living donation in part because of concerns involving and possibly risking the health of a living donor, pain related to the donor surgery, the possibility of kidney rejection, and an inability to ask someone to be a living donor [7,8].

DEPRESSION

End-stage kidney disease and transplantation are associated with depression [9], which impacts adversely upon compliance and may be associated with decreased longevity [10-12]:

- In a series of 209 consecutive primary renal allograft recipients, suicide accounted for 15 percent of deaths at 2.5 to 7.5 years of follow-up [13].
- In another study, the crude suicide rate in kidney transplant recipients from 1995 to 2001 was 24 per 100,000 patient-years, a finding that was 84 percent higher than the general population [14]. In multivariate models, age greater than 75 years, male sex, White or Asian race, geographic region, alcohol or drug dependence, and recent hospitalization with mental illness were significant independent predictors of death as a result of suicide.

In the kidney transplant population, depression occurs early after transplantation and is also associated with both acute and chronic rejection [15]. In one study, for example, patients with failed renal allografts were significantly more depressed, perceived less benefit from the treatment regimen, and had less confidence in their care providers than recipients of successful grafts [10].

Depression is also common in recipients of other organ transplants. Among heart transplant patients, for example, the incidence of depression was as high as 17 percent in the first posttransplant year [16].

The specific factors that increase a heart transplant recipient's risk for depression and anxiety-related disorders include the following [16]:

- Pretransplant psychiatric history
- Poor social support
- The use of avoidance coping strategies for managing health problems
- Low self-esteem

Other factors that may lead to depression include the disfiguring effects of immunosuppressive medication, such as high-dose glucocorticoid therapy, and antihypertensive treatment with beta blockers. (See "Major adverse effects of systemic glucocorticoids" and "Major side effects of beta blockers".)

Drug treatment — Previously, therapeutic options for depression were hampered by the side effects associated with traditional agents. By comparison, newer antidepressant medications are more effective and safer in both the general population and medically ill patients [17,18]; however, there is little published data concerning their use in allograft recipients.

This diverse group of compounds possesses distinct pharmacokinetic properties which are unrelated to either the tricyclic/tetracyclic antidepressants or the monoamine oxidase inhibitors. These newer agents include selective serotonin reuptake inhibitors, such as fluoxetine, paroxetine, sertraline, trazodone, and fluvoxamine. Agents with serotonin reuptake activity that also prevent the uptake of other neurotransmitters (such as norepinephrine and dopamine) include nefazodone, bupropion, and venlafaxine.

One problem associated with the use of these agents may be drug interactions resulting in elevated calcineurin inhibitor levels due to alterations in the cytochrome CYP3A4 isoenzyme system [19].

However, it would be an oversimplification to suggest that a drug is metabolized by only one specific enzyme.

Caution therefore dictates that levels of affected drugs should be carefully monitored in any transplant patient who requires treatment for major affective disorders. Appropriate dosage adjustments should be performed as necessary to circumvent toxicity.

BIPOLAR DISORDER

Long-term lithium use in some patients is associated with onset of chronic kidney disease, which may occasionally progress to end-stage kidney disease. (See "Renal toxicity of lithium", section on 'Chronic interstitial nephritis and kidney function impairment'.)

For patients with bipolar disorder who undergo kidney transplant as a result of end-stage kidney disease secondary to lithium, optimal maintenance pharmacotherapy for bipolar disorder is not clear. Using a drug other than lithium can put patients at risk for recurrences of major depression and mania, because alternative regimens may be less effective. Lithium has been used with caution after kidney transplantation, with the understanding that the nephrotoxic impact of lithium generally takes decades to manifest. There are few published data that describe the outcomes of lithium-treated bipolar patients after kidney transplantation.

POSTTRAUMATIC STRESS DISORDER

The evidence suggests that posttraumatic stress disorder (PTSD) is not a contraindication to kidney transplantation. As an example, a retrospective study of a nationally representative cohort of military veterans identified transplanted patients with a prior history of PTSD (n = 282) and a control group of transplanted patients without PTSD (n = 560) [20]. Patients were matched on variables such as age, type of donor, and comorbid diabetes; propensity scoring was used to match the two groups with regard to other observed potential confounders (eg, severity of general medical disorders, smoking status, and depression). The analyses found that all-cause mortality, death with functioning graft, and graft loss were each comparable for the group with PTSD and the controls. In addition, post-transplant medication adherence was comparable.

NONADHERENCE

Nonadherence with diet and medication is a significant problem among some transplant recipients. This is due to numerous causes, including psychiatric disturbances, adverse effects

of medications, lack of knowledge concerning the need for medications, and financial concerns [21]. This problem is particularly prevalent in children [22].

Nonadherence is one of the more important risk factors for acute rejection and graft loss [23-28]:

- In one study, the risk of acute graft rejection was 4.2 times greater among recipients who were not compliant with medications [28].
- Although the exact risk is difficult to assess, the odds of allograft failure may be seven-fold higher among noncompliant versus compliant patients [26].

Certain subgroups of transplant recipients have an enhanced risk of nonadherence [10,21,29-32]. One large study attempted to identify such risk factors in over 1400 patients who answered a questionnaire concerning whether they had missed one or more doses of immunosuppressive medications [29]. Multivariate analysis found that nonadherence was significantly associated with white collar occupations and a longer period of time elapsed since the transplantation, while compliance was most commonly observed among older patients and those who think that immunosuppressive drugs are highly important and exist in the body for only a short time.

An overview of the literature reported that certain patient characteristics were closely linked to nonadherence among solid organ transplant recipients [33]:

- Younger and older age, and non-married
- Anxious and individuals prone to denial, as well as those with severe personality disorders or intellectual disabilities
- History of substance abuse

Additional factors underlying adherence include the particular transplant center and dosing frequencies of immunosuppressive medications, with higher dosing frequencies resulting in decreased adherence [32,34].

Retransplantation among patients with allograft loss due to adherence can be difficult to justify due to concerns of repeat noncompliance resulting in the loss of the second allograft. However, if properly rescreened, there is some evidence that retransplantation among such patients can be successful. In a single center retrospective study, the outcomes of patients who lost their initial allografts to noncompliance and underwent retransplantation after a thorough evaluation were compared with a control group of retransplant patients who did not lose their initial grafts

to noncompliance [35]. At eight years, both groups had similar allograft and patient survival rates as well as incidence of chronic rejection.

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, “The Basics” and “Beyond the Basics.” The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the keyword(s) of interest.)

- Beyond the Basics topics (see "Patient education: Heart transplantation (Beyond the Basics)")

SUMMARY

- Although follow-up of kidney donors shows that the majority of individuals express positive feelings about having donated a kidney, kidney recipients have difficulty asking a possible living donor to donate a kidney because of concerns about risking the health of a living donor, pain related to the donor surgery, and the possibility of kidney rejection. (See 'Psychological impact of transplantation' above.)

- End-stage kidney disease and transplantation are associated with depression, which decreases adherence to treatment and may be associated with decreased longevity. Depression occurs early after transplantation and is associated with both acute and chronic rejection. (See 'Depression' above.)

- Depression is also common in recipients of other organ transplants. As an example, the incidence of depression among heart transplant patients is 17 percent in the first posttransplant year. Risk factors that increase a heart transplant recipient's risk for depression and anxiety disorders include pretransplant psychiatric history, poor social

support, using avoidance coping strategies for managing health problems, and poor self-esteem. (See 'Depression' above.)

- Selective serotonin reuptake inhibitors are often used to treat depression, but may interact with and increase calcineurin inhibitor serum concentrations. (See 'Drug treatment' above.)

- Transplant recipients may not adhere to their prescribed diet and medications, which may lead to acute rejection and graft loss. Risk factors for poor adherence include psychiatric problems, adverse effects of medications, higher dosing frequency of medications, lack of knowledge concerning the need for medications, financial concerns, white collar occupations, and a longer period of time elapsed since the transplantation. (See 'Nonadherence' above.)

- We encourage you to print or e-mail the patient information topic on heart transplantation. (See "Patient education: Heart transplantation (Beyond the Basics)".)

Topic 4850 Version 17.0