

FAST FACTS AND CONCEPTS #273 TREATING DEPRESSION AFTER HEART TRANSPLANTATION

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Background Mood disorders such as depression are some of the most common psychiatric illnesses seen in cardiac transplant patients (1). This *Fast Fact* discusses major depressive disorder (MDD) after heart transplantation. **Note:** many of the drug interactions discussed here are relevant for antidepressant therapy after most solid-organ transplants for which similar immunosuppressants are used.

Depression After Cardiac Transplantation MDD post-cardiac transplant often does not manifest with “classic” symptoms like anhedonia or tearfulness. Instead, it appears as regression, agitation, withdrawal, demanding behavior, and irritability (2,3). Depression is more likely if the patient had a mood disorder pre-transplant, if he/she has poor social support, if the pre-operative expectations were overly optimistic, or if there are significant changes in family and caregiver dynamics post-transplant (2,3).

Pharmacologic Therapy Treating depression in this patient population is challenging due to drug interactions from patients’ anti-rejection medications. For example, cyclosporine and tacrolimus are both metabolized utilizing the hepatic CYP450 3A4 pathway. Inhibitors of this enzyme increase the risk of cyclosporine and tacrolimus toxicity. Conversely, medications that induce 3A4, such as many anti-depressants, create sub-therapeutic levels of these drugs, increasing the risk of graft rejection (4).

- **Selective Serotonin Reuptake Inhibitors (SSRIs).** SSRIs are the first-line treatment for depression in post-cardiac transplant patients, despite having varying degrees of inhibitory effects on P450 enzymes. Citalopram/escitalopram and sertraline are the preferred agents in transplant recipients because of their minimal drug interactions (5). Citalopram/escitalopram also have less risk for post-transplant drug-induced obesity and diabetes (5). Sertraline’s cardioprotective effects (vasodilation of coronary arteries and endothelium protection) may benefit post-transplant patients at risk for myocardial infarction or coronary artery disease (6,7). SSRIs to be avoided include fluoxetine (compromises steady-state cyclosporine plasma levels), fluvoxamine (has highest 3A4 inhibition among SSRIs), and paroxetine (has highest potential for causing discontinuation syndrome) (5,6).
- **Serotonin Norepinephrine Reuptake Inhibitors.** Venlafaxine can be safely used in most transplant recipients, as it has little potential interactions with medications metabolized by the P450 enzyme system. However, doses exceeding 225 mg elevate diastolic blood pressure in 9% of treated patients, so it should be used with caution in patients with hypertension (5).
- **Tricyclic Antidepressants (TCAs).** The cardiovascular toxicities (conduction delays, QT prolongation, orthostatic hypotension, atrial fibrillation) of TCAs are well known, but some studies have shown that the denervated transplanted heart is less sensitive to those effects than previously thought (6). Nortriptyline is the least likely to produce cardiac side effects (6). TCAs lower the seizure threshold, as do many anti-rejection drugs. TCAs should be reserved for treating refractory depression in post-cardiac patients (6).
- **Monamine Oxidase Inhibitors (MAOIs).** Because of their propensity to cause hypertensive crises and strong probability of drug-drug interactions, MAOIs are not an option in this population (5,6).
- **Other Drugs.** Mirtazipine is a second-line treatment for depression in post-cardiac transplant patients and should be reserved for those suffering from cachexia who may benefit from its appetite stimulating effects (5). Bupropion has no effect on serotonin reuptake and is a reasonable alternative for cardiac transplant patients who cannot tolerate SSRIs. However, because of its potential to lower the seizure threshold and increase the adverse effects of calcineurin inhibitors on the central nervous system, patients need to be assessed for immunosuppressant-associated neurotoxicity before starting bupropion (5). Nefazodone should be avoided in cardiac transplant patients with depression because of its 3A4 enzyme inhibition (5). Although up to 30% of transplant patients take St John’s Wort (*Hypericum perforatum*), it induces the 3A4 pathway and should be avoided (5,6).

Non-Pharmacologic Treatments Transplant patients may have unique issues, such as feeling profound guilt for the donor and/or other patients on the waiting list who did not survive (6). A course of interpersonal psychotherapy, coupled with SSRI therapy, is effective in treating depression in cardiac transplant patients (8,9). Mindfulness-based stress reduction techniques have also been shown to decrease depressive symptoms and increase quality of life in solid-organ transplant patients, retaining benefits for at least 1 year (10). Electroconvulsive Therapy (ECT) is well known to be particularly effective and well tolerated in treating MDD refractory to pharmacologic treatment (6).

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