Mood Disorders in Transplantation: Depressive Disorders

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Thomas Soeprono, R. Michael Huijon, and Spencer Lunbeck

Introduction

Among transplant patients, depressive disorders are the most common psychiatric comorbidity [1]. Although rates of depression vary between different types of organ failure, they can be as high as 60% following organ transplantation [2], significantly higher than in the general population and even above those found in other medically ill populations [3, 4]. Risk factors associated with depression in the transplant setting are similar to risk factors for depression in the general population and include prior psychiatric history, length of hospitalization, level of physical dysfunction, and limited social supports [3]. Risk factors appear to be cumulative; the more risk factors, the higher the risk for onset of depression. The risk for depression also appears to be greatest during the first post-transplant year and may be attributable to the many stressors experienced during early recovery: physical deconditioning, adjusting to transplant directives and immunosuppressive medications, and transition from a state of illness to resuming prior roles and responsibilities [3]. Other risk factors especially relevant in the perioperative period in transplant are as follows: age, low socioeconomic status, length of hospital stay, graft versus host disease, low quality of life, impaired social functioning [5], side effects from immunosuppression medications [6], and length of wait for transplantation [7].

Depression is an independent risk factor for functional disability post-transplant [8]. Importantly across all organ types, depressive disorders and depressive symptomatology either pre- or post-transplant are associated with an increased relative risk of mortality of 65% and in kidney recipients appears to increase the risk of graft loss [9]. No studies have examined a mechanism by which depression may contribute to poor outcomes, although several studies suggest that adequate treatment of depression may improve medical surgical outcomes [10].

Lower or suboptimal adherence with medications and medical recommendations is often feared to be the behavioral link between depression and poorer post-transplant outcomes. Depression may contribute to nonadherence and is associated with difficulties in medical engagement [11]. While depression is an independent risk factor for increased morbidity and mortality after transplant, a relationship between depression and nonadherence to transplant immunosuppression medications has not been established [2]. In addition, it should be remembered that despite commonly attributing nonadherence to a depressive disorder, difficulties adhering to medical recommendations are more commonly rooted in behavioral patterns and environmental barriers within a patient's life. In the case of poor adherence, a thorough evaluation for depression and other potential psychiatric disorders is recommended to assess possible etiologic factors. Treatment of depression when present can remove this confounder and can improve adherence by reducing the neurovegetative symptoms.

Case History

Alejandra is a 48-year-old female with a history of type 2 diabetes and hypertension. She presents to the transplant clinic with end-stage renal disease after being on dialysis for 2 years. She hopes to obtain a kidney transplant so that she can return to work, be a more involved parent, and improve her relationship with her husband. They have two elementary-school aged children. Her loving and supportive family remind her to take her medications daily. Historically she has had difficulty with adherence to medications when she was still working because she had no scheduled breaks and would get "too busy."

But since starting dialysis she has had to quit work and misses having a daily schedule and "purpose." Now she falls

T. Soeprono (✉) · R. M. Huijon · S. Lunbeck
Department of Psychiatry, University of Washington, Seattle, WA, USA
e-mail: Thomasms@UW.edu; mikehuij@UW.edu; slunbeck@UW.edu

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asleep watching TV at night, sometimes without having taken her evening medications. She denies any substance use history other than having a "wild streak" in her twenties when she was in college. She denies any legal history or exposure to violence or abuse. She suspects that her older brother suffered from depression and that her mother has anxiety, but they were never formally diagnosed and never talked about it because "that's not done in my family."

She reports having first experienced depression in her teens in the setting of obesity and bullying at school but received no formal psychiatric treatment at that time. After the birth of her second son, she experienced in 2–3 month period of feeling down and unmotivated with significant worries that she was an inadequate mother. She received counseling from her priest for a 2-month period which she felt was helpful.

Prior to her transplant evaluation appointments, Alejandra filled out a Patient Health Questionnaire-9 (PHQ-9) which put her in the moderate range for risk of depression. Her most notable symptoms were daily challenges with sleep, energy, appetite, and concentration. This "positive" screen triggered the scheduling of an evaluation by a transplant psychiatrist. The scheduler noted that the patient was resistant to a psychiatric appointment stating that all the symptoms noted in the questionnaire were due not to depression but rather to her kidney disease and dialysis.

Since initiating hemodialysis she has been experiencing anhedonia, reporting that she can no longer participate in activities that she used to love. She recalls previously enjoying bike rides, now limited by her low energy, and traveling, now restricted by the stringent requirements of dialysis. She reports difficulty initiating sleep as a result of worrying about her health and that she might leave her children motherless. Even worse, she wakes up early in the morning "for no reason" and cannot get back to sleep despite staying in bed for many hours. She is not able to sit through an entire movie because she loses track of the plot and becomes disinterested. Although she continues to struggle with her weight, she reports having little to no appetite. She feels tired all the time but especially after dialysis. She denies any desire to be dead but sometimes wonders what the point of living is in her current situation. In her dialysis she notices when other patients suddenly "disappear" and never return. She wonders if or when this might be her story. She feels worthless and believes she has become a burden to her family.

She denies any need for a medication to help with her mood stating, "I don't want to change my personality." Although she is open to counseling given her success in the past with this type of treatment, she notes that she already has too many appointments as-is and adding another one each week would only make her life more difficult. Furthermore, she says that her depression is "situational" and that were it not for her kidney disease and hemodialysis, she would not be depressed. With the suggestion of psychotherapy to provide a time and space to process the stress, she refuses saying "I have all the support I need. Nothing anyone can tell me will make this go away." She adds, "if I could just get a transplant, this would all just disappear."

Clinical Questions

1. What are the best diagnostic methods or tools to assess depression in transplantation patients? Should transplant centers consider screening for depression?
2. In which scenarios should a patient with depression in the transplant setting be required to undergo psychiatric treatment prior to being listed for transplant?
3. What factors would deem a patient with a history of depression as an acceptable candidate for transplant listing?
4. What factors might mitigate risk for a patient with a history of depression?

Discussion

Evaluation of Depression in Transplant Candidates and Recipients

As in the example case, patients in transplant process can be identified for psychiatric evaluation through numerous pathways including medical history found by transplant coordinators, screening tools, and referrals from the multidisciplinary transplant team.

Some transplant programs use screening tools for all candidates as one method of identifying patients who may benefit from an evaluation by a mental health professional. Screening tools do not establish a diagnosis however can be helpful in targeting individuals who are at higher risk of depression. These tools have been helpful in creating a common language and format for psychiatric evaluation and the transplant setting—but they do not substitute for professional psychiatric evaluation and treatment [12]. A patient who screens positive is typically referred to a mental health clinician familiar with transplantation for a more in-depth evaluation with a clear understanding of the comorbidities and presentations of illness in transplant. Only over repeated visits do these measures help providers in guiding diagnosis [13] or evaluating response to treatment.

Screening tools for depression include Patient Health Questionnaire-9 (PHQ-9), Beck Depression Inventory (BDI), Beck Depression Inventory for Primary Care (BDI-PC), the Hospital Anxiety and Depression Scale (HADS), and the Depression in the Medically Ill-18 (DMI-18) all meant to assess patients in more medically intense scenarios. The BDI-PC is differentiated by its complexity and is considered burdensome to many practitioners despite

it consisting of only seven questions. HADS centralizes anhedonia in the conceptual framework of depression which can easily be misunderstood in the transplant population when clear physical limitations as a result of organ failure inhibit participation in pleasurable activities. The PHQ-9, although very specific for depression, relies heavily on neurovegetative symptoms which as previously discussed are common in end-organ failure and may confound the diagnosis. The DMI focuses more on affective symptomatology and is somewhat less prone to influenced by physical symptoms; therefore, it stands out for its sensitivity in medically ill patients [14].

Evaluation of depression in the transplant setting can be difficult as a result of significant impairments in end-organ disease. Severe lethargy, anorexia, insomnia, and impaired concentration are typical signs and symptoms in this setting [8]. These neurovegetative symptoms can both cloud the diagnosis of depression and masquerade as a depressive disorder.

A clinical history and exam by an experienced mental health professional with extensive experience in transplant remains the most effective diagnostic approach [15]. Transplant psychiatrists have seen common patterns in the manifestations of depression in end-stage organ failure that can be difficult to separate from the symptoms associated with organ failure. The following paragraph will differentiate these similarities and differences, focusing sequentially on the symptoms associated with major depressive disorder.

Anhedonia is one of the most frequently misunderstood symptoms among transplant patients. The dictionary definition of anhedonia is focused on an individual's capacity for pleasure. The PHQ-9 asks if patients have had "little interest or pleasure in doing things." The most common response to this question is generally "I can't do anything." This makes ascertaining a person's capacity for pleasure difficulty when there are no outlets for pleasure. The true physical limitations of organ failure force mental health practitioners to glean a patients overall pleasure from the day-to-day activities or ask the patient to imagine participating in an activity, both of which can be suspect from a diagnostic standpoint.

Hopelessness and feelings of depression are quite common as discussed in epidemiology above. The most frequent response in the transplant setting to inquiries of this nature is "who wouldn't be?" This brings up the very real and hard truth that transplant candidates face which is that risks with organ failure and organ availability are dire. Mental health practitioners in transplant must walk a fine line between validation of the dismal statistics, realistic expectation setting, and bolstering resilience and hope in extremely challenging circumstances.

The neurovegetative symptoms of depression (appetite, sleep, energy) are so common in organ failure that it is probably more significant when individuals deny any issues with them. At the same time, many of these symptoms, especially sleep difficulties, often pre-date their need for transplant. As a result, practitioners must have realistic expectations for treatment before and throughout transplant. Even when the neurovegetative symptoms are rooted in end-stage organ disease rather than depression, patients can benefit from pharmacologic, psychological, and behavioral treatment strategies.

Organ failure can often bring with it serious feelings of guilt and regret because of past behaviors such as alcohol use, smoking, and medical nonadherence that contributed to their disease. Similarly, to addressing feelings of hopelessness, the provider must strike a balance between validation, a supportive stance, and providing realistic and truthful feedback. In the post-transplant period, the survivor guilt is often described. Three common cognitive schemas are contributing to the post-transplant survivor guilt: the regret over self-inducing illness by substance misuse or unhealthy lifestyle, the preoccupation that "someone died for me to get a transplant" and the guilt about being the one to eventually receive a graft while many transplant candidates die on the waiting list.

Organ-Specific Presentations of Depression in Transplant Candidates and Recipients

The diagnosis of depressive disorders in transplant candidates is challenging because of the overlay of both neurovegetative and psychological symptoms common to both end-state organ disease and depression. The stressors of the transplant process, social disruption because of illness, and grief associated with morbidity and potential mortality in organ failure contribute to feelings of depressed mood, guilt, and anhedonia, with similar phenomenology to major depressive disorder. Although both depression-specific tools such as the DMI-18 and transplant-specific tools such as the SIPAT can augment a psychiatric evaluation and provide supplemental information in a structured format, ultimately a thorough diagnostic interview by a skilled transplant psychiatrist is the best evaluative practice.

Each organ system has a unique clinical presentation of depression based on the common symptoms and challenges that occur within organ failure of that system. Patients with kidney failure experience a protracted course of demoralization in the setting of years on dialysis or on the kidney transplant list. Although dialysis is a wonderful life-saving treatment, it also is a heavy burden that makes employment and life schedules difficult to maintain leading to nearly 50% of patients on dialysis to develop depression [16, 17]. Patients with end-stage renal disease may endure years of dialysis that cause significant dysfunction in their professional and social life leading to profound isolation. Without work or

school, lack of structure may progress to unhealthy circadian rhythms and depression. In the setting of dialysis and end-stage organ failure, depression is common, but often attributed to the chronic course of the general medical condition [18]. Long-term dialysis patients speak of the grief experienced after the sudden disappearance of a dialysis neighbor.

Individuals suffering from liver failure as a result of substance use often suffer from comorbid-limited coping strategies to confront the significant stresses in the transplant process. These less adaptive means of managing stress, previously hidden by misuse of alcohol, often lead to depressive symptomatology when these patients with liver disease come under the strains of transplant evaluation and declining function. Decreased concentration is a common characteristic of hepatic encephalopathy regardless of the etiology of the liver disease [19]. These cognitive impairments should not be misdiagnosed as depression but may limit an individual's capacity to participate in psychotherapy, develop new coping skills, and practice behavioral activation for treatment.

Both lung and heart transplant patients experience profound exhaustion and inactivity that result in deteriorating moods and isolation from social networks. Although patients will frequently endorse anhedonia when asked directly, it is more often the case that they can no longer participate in their activities from the past. Having the desire to do something without the capacity can cause stress and feelings of dislocation, disconnection, and resentment when these individuals attempt to relate to their peers. Deconditioning, anorexia, and lethargy present a continual battle for patients suffering from lung and heart failure. In patients with heart failure, depression has greater impact on quality of life measures than the patient's ejection fraction [5].

All organ failure patients express an experience of distancing from "regular" people in social settings. They experience quotidian, mundane troubles such as getting stuck in traffic or a mishandled restaurant order as so insignificant in comparison to their worries that they may experience unusual anger and guilt. The anger often stems from feeling slighted by their friends who do not realize what monumental stress they are under, while guilt is rooted in both knowing that they themselves were once focused on "minor" matters and feeling that they cannot be the empathic friend that they strive to be.

In the postoperative period, depression can manifest through guilt related to organ allocation. Recipients may feel that "someone had to die for me to live." Another presentation of this guilt takes on a utilitarian form "I'm not doing my organ justice because I'm not living up to my full potential." Both are clear cognitive distortions and may be rooted in post-transplant depression. A thorough evaluation and discussion of the factors underlying the patient's concern are core features of not just assessment but treatment of this guilt. A frank discussion and realigning of expectations under a patient's current circumstances that may have changed because of complications can allow a patient to more accurately engage in reality testing and feel grounded. Empathy and validation of a patient's concern while providing a clear behavioral pathway to recovery can adequately address the patients concerns and initiate change.

Other Depressive Disorders

There are other depressive disorders other than major depression that afflict transplant patients. Initially, many patients in this setting present with an adjustment disorder, most often in the case of a rapid or dramatic decline in function. As the diagnostic name implies, this can be a matter of adjusting to these significant changes. In these cases, symptoms will often resolve with no intervention other than appropriate support and education. Participation in the transplant evaluation process can also overwhelm patients and precipitate an adjustment disorder [2].

Patients can experience demoralization on the other end of the transplant process as well, often thought of as a depressive "diagnosis of attrition." These demoralized individuals present with clear depressive symptoms, which patients can mask and are much more affectively reactive in specific scenarios around loved ones. Demoralization is amenable to supportive psychotherapy, support, and validation, whereas psychotropic medication tends to be less effective [20, 21].

Some depressive disorders have much more chronic courses such as in dysthymia. A patient may have suffered with chronic depression for a long time but his/her first interaction with a psychiatrist may occur in the transplant evaluation process. This could be the initial identification of a long-term depressive disorder that has influenced the patient's thoughts, feelings, and behaviors for the past decades. In this setting, realistic expectations about treatment and over what time course should be set. At the same time, substantial improvement can be made with simple interventions and thus should not be delayed to the post-transplant period.

Substance-induced mood disorders have been known to persist for up to 1 year after the cessation of substances. More importantly, persistent and heavy substance use that contributes or precipitated organ failure also impairs the individual's capacity to develop alternative and more adaptive coping strategies. These skill deficits put the patient at a disadvantage as they attempt to psychologically manage the stressful process of transplant. This process in turn puts individuals at higher risk of relapse and is discussed in much more depth in other chapters.

Lastly, there are depressive disorders due to general medical conditions. This may often be further complicated by the numerous medications that transplant patients are on that can affect one's mood. As examples, steroids, immunosuppressants, and antiepileptic medications are all well known to

cause or contribute to psychiatric symptoms. On the other hand, there continue to be misunderstandings about common medications such as beta-blockers, which are falsely thought to precipitate depression [22].

In our case, the patient cites her kidney illness as the primary contributor to the decline in her mental health. On initial evaluation, it is difficult to discern the origin of her symptoms. Upon further questioning, it becomes clear that she is experiencing notable psychological symptoms well beyond the neurovegetative symptoms. In the case that psychological symptoms persist and contribute to impaired function, further evaluation and treatment must be pursued. Because she has a rather robust social support network and no outstanding red flags in terms of substance use, she could easily go undetected—and as a result untreated—if a screening tool was used in isolation. As previously stated, the screening tools although not diagnostic are often utilized by transplant programs in an effort to make the ambiguous concrete. This example is meant to demonstrate an inappropriate use of similar measures which can lead to oversimplification of the interplay of psychosocial factors in transplant and specifically its impact on depression. Ultimately, no assessment measure outperforms a thorough and complete psychiatric interview and physical exam in the evaluation of depression.

Depression in the transplant setting is unique as it can parallel the patient's progression throughout the transplant process [23]. In pre-transplant evaluation, patients are expected to complete a lengthy list of medical assessments and testing that can be uncomfortable and demanding. Once approved and on the transplant list, the waiting period can precipitate diminished participation in life activities for fear of missing "the call" [6, 24]. Patients experience insomnia from worry and medications such as steroids. Postoperatively, patients expect that the struggles that they confronted before transplant will quickly resolve after receiving their graft. They can become demoralized when they find that many of these same challenges persist despite improved physical health and normal organ function. Increased levels of stress have clear correlations with rates of depressive disorders [25]. Transplant centers have an imperative to provide mental health support given the known, expected stress that every transplant candidate will endure throughout the process. Appropriate evaluation and treatment of depressive disorders can lead to improvements in transplant outcomes.

Suicidality in Transplant

Evaluation of suicidality is especially challenging in the setting of organ failure. The lives that patients with organ failure lead are difficult and are experienced as not worth living at many times throughout the course. Suicide is a significant risk in the general population—let alone those with organ failure who are under disproportionate stress with limited options. As a result, transplant professionals have reasonable fears of suicide in their patient population. Aside from the obvious concern for each patient under their care, transplant centers also have an obligation to ensure appropriate stewardship of limited organ allocation [26]. Suicide is not only the loss of the individual's life but also a loss of a potential "other patient's" opportunity for a better and longer life. Suicide in a transplant patient can have long-lasting and ripple effects throughout the transplant community. This is not to say that individuals with suicidal ideation should not be transplanted. Rather, individual who suffer from this affliction need to be aware of protective resources, be willing to reach out for help when needed, and demonstrate an open and honest line of communication with their practitioners. Many patients have difficulty navigating between honesty with providers in expressing normal hesitancy and fear about the realities of their health condition. At the same time, patients must attempt to maintain the hope and drive necessary to get through transplant to enable them to return to a life that is worth living.

In the example case provided, the patient has wishes of being dead, commonly called passive suicidal ideation. She seems to be relating with her peers from dialysis who die, and she never hears from again. These escape fantasies are common in chronic illness where life satisfaction is low, and patients perceive themselves to a burden to those around them. This is not especially concerning from a safety standpoint but can cause transplant teams hesitation given the risk to the scare resource they manage. Appropriate evaluation and safety planning are warranted while providing reassurance and clear assessment to the selection committee.

Evaluation of suicidality can be further complicated by historical/remote suicide attempts. The appropriate length of time or criteria necessary to reassure a transplant team that suicide is not likely in the future is still not clearly established [12, 27]. Rather these instances are evaluated on a case-by-case basis taking into consideration numerous factors including but not limited to social support, coping strategies, recency, ongoing mental health treatment, and severity of attempt. A prior suicide attempt alone should not be considered an absolute contraindication to transplant in and of itself. As with all suicide assessments, the thoughts and actions must be placed into a context with risk factors while seeking to understand motivation and protective forces [27, 28]. See the chapter on suicide for more information.

Treatment of Depression in Transplant

Our example case depicts an individual who is suffering from major depressive disorder, moderate, single episode in the setting of the long-term sequela of kidney failure. Dialysis has precipitated isolation and perceived

purposelessness in life. Despite this, our patient ultimately has low risk of long-term psychiatric illness and expected rapid recovery with appropriate psychiatric treatment if she receives treatment for her current depression.

Our sample highlights a common and challenging situation in addressing depression in the transplant setting. Many patients understandably see their organ failure as the primary driver of their mental health decline; they then draw the plausible but erroneous conclusion that their mental health will suddenly improve post-transplant. This is sadly not usually the case. More importantly, patients cannot know how long their wait for an organ may take. Optimism, although helpful, can also contribute to distorted cognitions and impair a patient's ability to participate in realistic treatment planning. What starts as a mild depression can turn into a severe depression over the course of stressful years waiting on the transplant list and going to dialysis while friends and family live life like nothing has changed. Clinicians can improve patient participation in realistic treatment planning—including early treatment of depressive symptoms—by working with patients to set the appropriate cognitive framework: transplant is a lengthy process, not an event.

Both practitioners and patients accurately see depression as a potential contraindication to transplant candidacy if left untreated. As a result, patients may guard against full disclosure of their psychological state. Without objective measures of depression, mental health providers can be limited by the report of the patient if evaluated alone. Patients may be motivated to "fake it" throughout the evaluation for fear of repercussions on their candidacy. Of course, collateral information can help provide a more holistic picture, but family and friends may also be complicit for similar reasons. Implicit bias against psychiatric illness among medical providers and patients can limit access to mental health care within the medical system. For these reasons, any reassurance surrounding a patient's candidacy that can be given should be given. Furthermore, discussions surrounding the potential risks associated with untreated mental illness and an earnest expression of concern for the patient's overall health in every realm even outside of the transplant setting can build rapport and engagement that minimizes the restraints noted above.

Treatment of depression in the transplant setting should align with the standard practice for depression treatment in the general population. There are a few additional considerations for mental health providers in the transplant setting surrounding psychopharmacology. It should be anticipated that antidepressant medications will be needed by a patient with organ failure or on immunosuppressant medications. Understanding and carefully checking drug—drug interactions is imperative for the safety and health of transplant patients. Understanding the metabolic pathways of the most utilized immunosuppressants is invaluable to providing safe depression treatment.

Sertraline, citalopram, and escitalopram are the mainstays of antidepressant treatments in the transplant setting as a result of their minimal risk of drug—drug interactions and favorable side effect profile [29]. Citalopram should be avoided in patients with higher cardiovascular risk due to QT prolongation. In liver failure, dosing of all antidepressants should be adjusted accordingly. Bupropion is often considered an augmenting agent in transplant because of its stimulating effects, and as a safer alternative to psychostimulants, which are used sparingly. Venlafaxine and mirtazapine are excellent alternatives when the aforementioned agents prove to be in effective [29]. Fluoxetine, fluvoxamine, paroxetine, and duloxetine are the antidepressants most avoided in the transplant setting because of drug—drug interactions, tolerability, and risk of hepatotoxicity. For a more detailed discussion of psychopharmacology in transplant patients, please review the chapter by Gamboa et al. [30].

Antidepressant treatment is indicated at the very least for treatment of moderate to severe depression [29]. However, often in the transplant setting, patients can benefit from antidepressants even in very mild cases where the expected medication profile or side effects are leveraged to treat the consequences of organ failure or other comorbidities. An example would be the use of mirtazapine to address both depression and weight loss from poor appetite in the setting of ascites and liver failure. Another example might be the use of bupropion to treat depression and help with smoking cessation in preparation for lung transplant.

Psychotherapy is recommended for mild to severe depression in the case that a patient can continue to participate in treatment safely [31]. It is especially thought to be a very safe and less intensive method of treatment for mild depression, although there are clear limitations. Denial of severity of illness, lack of emotional vocabulary, and high symptom burden are all known to be associated with worse depression scores [32]; psychotherapy can provide a forum to address each of these issues. The temporal strain associated with frequent psychotherapy treatment can provide significant burden to patients whose lives are already dictated by medical appointments. To address the risk factor of diminished physical activity, behavioral activation and physical exercise are recommended but limited by physical dysfunction in the setting of organ failure [32]. As a result, the treatment of depression throughout the transplant process is often challenging and requires a multipronged and iterative approach. Unfortunately, access is poor to repeated psychiatric care, beyond consultation and evaluation for transplant candidacy alone [33]. Regardless, psychotherapy remains a mainstay of depression treatment and with a solid therapeutic alliance yields excellent results.

When patients are able and willing, psychotherapy can provide significant benefit in the case of demoralization and adjustment disorders. The supportive process, time, and

psychoeducation are active ingredients in the setting of a trusted therapeutic relationship. This can also provide a much-needed respite for caregivers who are often as exhausted as the patients throughout this long process. This is in contrast to antidepressants, which are not considered effective with a low level of evidence for use in these more mild and brief pathologies [34].

Especially in the physically ill, behavioral and social treatments of depression can be especially effective. Many organ failure patients are homebound without strenuous effort and assistance from caregivers. Regular exercise—or even just getting out of the house—can provide significant psychological benefits [35]. Because of the impairments in metabolism with liver disease and filtration with kidney disease, diet can have enormous impacts on a patient's function and mood. Active engagement with a transplant nutritionist in combination with behavioral changes can provide benefits not only to the patient's mood but also to the long-term health and success of the patient even post-transplant. Lastly, socialization is imperative for these patients who spend most of their time isolated due to their illness. Engaging family and friends in a regular visit schedule can lift a patient's spirits, give a patient's day some structure, and provide an outlet for reflection and stress.

As in the case provided, engagement in mental health treatment is often the biggest hurdle. Each patient has his/her own beliefs and bias surrounding mental illness, which impact the acceptable options for treatment. Cognitive deficits and physical disability may decrease patient's ability to participate in routine psychiatric interventions such as psychotherapy. Patients should be encouraged to utilize any existing social supports, both to optimize transplant outcomes and for effective treatment of depression. Often patients with end-stage organ disease experience challenges to physical strength, cognitive space, and daily routine which hamper their ability to follow through on depression treatment plans. Incorporating family and friends into behavioral activation practices can be one tool to overcome these barriers. At the same time, in the transplant setting, patients are very motivated to follow through with medical recommendations; this can be leveraged to the benefit of depression treatment. Just like in other mental health treatment settings, psychoeducation can go a long way in both treating the patient and increasing the motivation for treatment. A combination of biological, psychological, behavioral, and social interventions makes for the most effective treatment approach.

Beyond the improvements to life satisfaction and quality of life associated with depression treatment, substantial concrete health factors can be improved by treating depression preoperatively [15]. Improved rates of adherence, shortened lengths of hospital stays, improved post-operative recovery, and most importantly mortality are all thought to be inversely correlated with severity of depression [9, 36–38]. Beyond survival, depression is an independent risk factor for functional disability after transplant, which clearly has implications for quality of life [8].

To minimize risk to transplant outcomes associated with depression providers should focus on identifying existing coping mechanisms, promoting adaptive and effective strategies, and assist patients with cultivating additional techniques.

Although the context in which depression occurs is extremely important, it is equally important to delineate the functional deficits that occur as result of these symptoms, regardless of specific etiology and precipitants. Often patients use context to explain their hesitation to seek psychiatric treatment.

Depression regardless of etiology warrants aggressive treatment in the transplant setting, especially when it is leading to functional decline and nonadherent behaviors that put their candidacy or graft at risk. Rolling with the patient's preferences for any given treatment approach in depression is helpful, in this setting as in any other. Given the high-stakes nature of the transplant setting, however, it is reasonable to collaboratively create explicit plans to review treatment progress with patients and agreed-upon timelines to consider alternative treatments. Doing so creates a pathway to more aggressive and effective depression treatment if needed.

Patients who exhibit comorbidities that are known to contribute to and perpetuate depressive disorders should be required to undergo more aggressive depression treatment and may be denied transplant candidacy until these factors are better addressed. Treatment refractory depression, concomitant poor self-care with limited social support, or patterns of nonadherence are examples of such issues. Repeated or severe past suicide attempts, personality disorders, or recent major losses (such as the death of a child) may warrant a period of mental health stability to assure the selection committee that the best outcomes in transplant are possible. Unfortunately, there are no distinct time periods at which anyone can fully predict ongoing resolution. But some specified period may allow the patient and transplant team additional time to form a functional working relationship. The relationship between substance use and depressive disorders, a frequent comorbidity, may need to be directly addressed and is covered more thoroughly in other chapters. The dearth of specific recommendations is the result of limited data on these issues in the transplant setting and how they directly impact transplant. As a result, there are no hard-and-fast rules or time scales to guide selection committees. Instead, the consultation of a transplant psychiatrist who has the experience and knowledge of mental health issues in the transplant setting has no substitute.

Under the time pressure and persistent symptoms of end-stage organ disease, it is common for patients to achieve only

partial resolution of their depressive disorders or to continue to experience persistent comorbidities. This also could occur in individuals with chronic and severe depressive disorders. In these difficult cases, a candidate with some combination of self-awareness, insight, understanding a clear pattern in their depressive episodes, willingness to seek help, a strong support system, trust in the medical system, and a relationship with a mental health professional can be an acceptable candidate for transplant.

Take Home Points

1. Stress related to the transplant process can precipitate depressive symptoms that warrant evaluation and treatment.
2. Screening for depression in transplant patients should be considered but final diagnosis should be based on a thorough psychiatric evaluation.
3. Treatment of depressive disorders using psychopharmacologic, psychotherapeutic, and behavioral strategies is recommended at any point throughout the transplant process.
4. Treatment of depressive disorders improves quality of life in transplant candidates and recipients.

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