

ARTICLE

Case Vignettes in Transplant Psychiatry Ethics

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Abstract

The demand for liver transplants continues to far exceed the number of available viable donor organs; hence, it is of utmost importance to determine those individuals who are best able to care for these valuable, limited resources as potential recipients. At the same time, psychiatric comorbidity is common in the course of end-stage liver disease and can be mutually complicating. This article focuses on liver transplant candidacy from a psychiatric perspective, using illustrative cases to underscore the foundational facets of medical ethics that serve as the guide to these complex medical and ethical decisions.

Keywords: organ transplantation; liver transplant; organ donors; organ recipients; transplant psychiatry; consultation-liaison psychiatry; transplant ethics

Selecting the appropriate transplant recipient is crucial from an ethical standpoint, as the number of needy individuals far outstrips the available viable donor organs. In the United States, while a candidate in need of organ transplant is added to a national waitlist every 10 minutes, an estimated 20 individuals perish awaiting a new organ daily¹. Hence, only those individuals who can best care for this precious, life-saving resource should be considered as potential recipients. Key to transplanted graft organ and recipient survival includes adequate immunosuppression, to prevent the host recipient body from attacking the transplanted organ as foreign invader. This is achieved pharmacologically via antirejection immunosuppressants, which require close monitoring and adjustment in the post-operative period. Estimates of psychiatric burden for liver transplant patients vary, but are thought to be significant—nearly two-thirds may suffer from depression,² while one-half may suffer from anxiety³—and others may develop neuropsychiatric issues through the course of liver illness that may impact their potential candidacy. Still others may have developed liver illness as a direct result of their psychiatric condition—considering substance use disorders within psychiatry, alcoholic cirrhosis is the top diagnosis for liver disease requiring transplant.⁴ Although further investigation is warranted for clarification, comorbid psychiatric disorders have been identified as the top risk factor for post-transplant resumption of alcohol use,⁵ and psychiatric illness may increase the likelihood of allograft loss by up to three to fourfold within the first year.⁶ Hence, psychiatric conditions play a significant role in the care of the liver transplant patient and may be a central focus of attention when considering patients for transplant candidacy. Likewise, the core tenets of medical ethics—beneficence, nonmaleficence, autonomy, and distributive justice—underlie every decision made as potential candidates are considered for placement on the transplant waitlist. The following cases are designed to highlight some of the ethical issues that arise in transplant psychiatry in consideration of patients for liver transplant. Although each case may lay focus on one of the four major ethical principles, in reality, multiple principles may be germane; the discussion afterward is likewise not meant to be complete, but merely a launching point for further consideration.

Case 1: A 28-year-old married military veteran, a mother of three young children, is admitted for acute liver failure resulting from intentional acetaminophen overdose. This is one of several lifetime suicide attempts dating back to her youth, wherein she was the survivor of repeated sexual abuse. As an adult, she

may have also suffered psychological trauma associated with her prior career in the military. She had sought psychiatric treatment in the past, but the consistency thought to be needed for sustained positive gains has been elusive due to geographical moves, poor adherence, and—in terms of medical care afforded to her as a veteran—ambivalent relationship with the military. Despite her difficult past, she has been reported by her husband to be stably married for some years, with the oldest of her young children approximately the same age as when the patient's abuse began. Other members of her family, however, describe a history of tumultuous relationships, periods of estrangement, frequently expressed wishes to die, and are perplexed by the patient's claims of childhood molestation, which they continue to doubt. The patient herself is transferred from a local hospital intubated for mechanical ventilation, due to hepatic coma as her liver function continues to decline; prior to losing consciousness, the patient expressed regret over her suicide attempt, and a wish to live for her children.

Comment: There is no doubt that, with prior history of suicide attempts, psychiatrically this patient would be thought of as a considerable risk for transplant candidacy. Active suicidal intent is obviously an absolute contraindication, as is the potential loss of a grafted organ via any other willful act after transplant—be it nonadherence to antirejection medication regimen, or resumption of alcohol or other substances that may lead to transplanted organ failure. Although the patient, in this case, regrets her most recent suicide attempt, her past of recurrent suicidal behavior would portend an elevated risk of similar attempts prospectively. But if we consider the source of her chronic self-destructive tendencies by suicide, prognosis may be less clear. Elements of the clinical information available suggest a diagnosis of borderline personality disorder, which, once thought to be indissoluble lifelong, has proven not only treatable, but perhaps prone to muting over time.⁷ Hence, as she ages, would this patient's psychiatric disease become less lethal? And, could she be considered less at risk to harm herself, and her transplanted organ, as time passes? On the other hand, the patient's presentation also suggests the possibility of post-traumatic stress disorder (PTSD), a disease that may also have a chronic course whose acute fluctuations may vary over time, and perhaps with less known tendency to improve.⁸ Elements of potential poor access, or adherence, to care, discrepancies in past history, potential bias from various family members, and an inability to speak directly to the patient, as may occur after severe overdose attempts, among others, also complicate this clinical picture. However, a correct diagnosis may seem very key psychiatrically—with an erroneous one potentially contributing to a wrongful denial of transplant candidacy on the one hand, and on the other, an extremely poor outcome (nonadherence leading to loss of graft organ, or suicide post-transplant) in an ill-suited candidate. Nonmaleficence, a central tenet of medical ethics, is often paraphrased as “do no harm;” in this case, the “do” may have less to do with treatment rather than diagnosis, and, most importantly, its anticipated prognosis. We have noted other specialties working with the transplant service be asked to predict the clinical future—for instance, for oncologists, the prospect of cancer recurrence in a transplant candidate with a past history of treated malignancy. For psychiatry, our ability to diagnose accurately is tethered to a diagnostic interview, often with the aid of appropriate scales⁹, neither of which are directly possible in this intubated patient; diagnosis remains phenomenologically based, where proven diagnostic testing (e.g., via lab test or imaging), rigorously tested for accuracy, remains elusive. In reality, our patients may carry multiple diagnoses—borderline personality, depression, and PTSD may often coexist¹⁰—and thus a prognosis ultimately varies by individual, and their unknown future. Fortunately, at our institution and others, the hepatologists and intensivists caring for these patients status post overdose are often able to help these patients overcome the toxic effects of the acetaminophen and miraculously avert the need for transplant altogether.

Case 2A: A 54-year-old man originally from Southeast Asia with a history of chronic hepatitis B is transferred into the intensive care unit with bleeding, acute kidney failure, and fluid overload due to end-stage liver disease. The patient had previously discussed the possibility of a liver transplant with his local hepatologist, and was in favor of such if medically necessary in the future. Upon interview shortly after transfer, however, the patient clearly states he does not want a transplant, despite the advice of his medical team and his tearful wife.

Comment: Transplant is, like many surgical interventions, an elective, life-saving procedure. Hence its informed refusal is perhaps one of the ultimate exemplars of the primacy of autonomy. From a more purely medical standpoint, this case is an example of the multiorgan effects of liver failure. Unbeknownst to us initially, the patient, an immigrant from where the hepatitis B virus may remain endemic, had also been suffering from a diminution of cognition due to hepatic encephalopathy (HE), a condition caused by excessive build-up of neurotoxic ammonia that the failing liver cannot adequately metabolize. HE can present dramatically, as in hepatic coma (as in the first case above), or more typically, with altered sensorium, but can manifest more subtly with an alert and oriented but nevertheless confused patient, and hence may be underdiagnosed.¹¹ Interview with an interpreter in the patient's primary, native language for the purposes of clarifying his medical wishes first suggested the presence of HE, confirmed via formal cognitive testing and physical examination. After treatment, consisting chiefly of osmotics that facilitate the elimination of excess ammonia, the patient's mentation returned to baseline, as did his informed autonomy, and he was resoundingly in favor of transplant if needed—more consistent with his prior opinion, and avoiding an ethical mishap with potentially fatal consequences.

Restoration to baseline mental status, however, is not always so rapid and facile, and consideration of autonomy can be less clear, as illustrated below.

Case 2B: A 34-year-old man originally from Central America with a history of chronic hepatitis C is transferred into the intensive care unit with ascites, hepatic hydrothorax, as well as hepatocellular carcinoma. He carries a diagnosis of intermittent anxiety, which subjectively worsens as the hospitalization progresses; hence his inpatient team resumes an antidepressant which he had previously been administered by his primary care provider. Some days later, psychiatric consultation is sought out for changes in mental status. We find the patient to be a wide-eyed, most enthusiastic interviewee, with rapid, loud speech interrupted by bursts of singing, an endeavor which the patient asks the team to join despite his shortness of breath. Simultaneously, his rambling narrative also describes attaining enlightenment during the course of this hospitalization, something he hopes to spread to the entire world, starting with us. His primary treatment team, along with one of his close friends at bedside, confirm his current mental status to be an abrupt change from baseline. The patient is accepting of pharmacologic treatment for this new-onset manic episode, but a few days later is demanding discharge, stating he no longer wishes to pursue a liver transplant. He is considerably less garrulous, but remains restless, and still far from his baseline mental state. He is, however, able to cogently describe his current medical condition, rationale for his decision, and its consequences, including death.

Comment: How much of this patient's presentation—most notably his change in wishes regarding transplant—is a result of his new-onset mania? We would tend to think significantly, as the difference between his current and past wishes regarding transplant would indicate. Mania, often characterized by restless distractibility, is hardly aligned with a prolonged medical hospitalization. Despite his change in opinion, the patient retains his ability to provide informed consent, and thus his decision at the moment—despite prior ones to the contrary—would need to be heeded. Departure from this hospitalization against medical advice may not preclude transplant in the future, but his chances of surviving until then are, per the primary treatment team, greatly reduced upon leaving the hospital. We are often asked in situations similar to these whether there are ways in which the patient may be detained from a psychiatric perspective. Involuntary detention laws in our jurisdiction are, as in many areas, based on criteria of dangerousness, either as a result of direct harm (via intent for suicide or harm toward others) or an inability to care for self, termed “grave disability,” as a result of psychiatric illness.¹² In cases of mania that do not involve suicidal intent or homicide, such as above, the only consideration might be for grave disability, which based on our experience would not be upheld by local adjudication—the patient, despite his manic symptoms, can describe a clear plan for self-care for basic necessities such as housing or sustenance. His potentially terminal medical condition would not be considered in this realm, medical informed consent being distinct legally from psychiatric incapacity. Similarly, psychiatric involuntary detainment would have little practical relevance to his potential transplant—hence even if he were

detained involuntarily from a psychiatric perspective, no procedures or treatments could occur against his wishes, assuming the patient maintained decision-making capacity for each treatment considered. Practically and ethically, the only hope involuntary psychiatric detention might afford would be to allow for enough time for his mania to improve (typically weeks, even months in length for complete resolution),¹³ with the hopes that he could reconsider his decision regarding transplant without the unquiet impatience of the mania. In rare instances, individuals with known bipolar disorder, or other conditions that may afflict a patient temporarily with poor judgment, might compose an advanced directive, to be enacted to override a potentially bad medical decision during psychiatric exacerbation.¹⁴ Our patient, having never previously suffered from major psychiatric illness save for intermittent anxiety, would not have known to prepare such a document. Likewise, the mania which curtailed his judgment might theoretically be considered to be of iatrogenic origin, as antidepressants in susceptible individuals are known to push, or “flip,” patients into mania, and hence potentially in the realm of malfeasance; it is a known risk to treatment, however, and antidepressant exposure may not elevate the risk of mania significantly as once presumed.¹⁵

Case 3: A 67-year-old married woman is being considered for second liver transplant some 11 years after her initial procedure for end-stage liver disease due to fatty liver disease and former heavy alcohol use. The cause of her fatty liver is theorized at least in part to be due to second-generation antipsychotics prescribed previously for a diagnosis of bipolar disorder type II. After the first transplant, treatment for her mood disorder is switched from antipsychotic to a mood stabilizer, with good efficacy. Local mental health care has proved difficult to obtain, hence the transplant psychiatry team has had intermittent clinical contact with the patient and her local primary care providers, who had assumed prescription of the mood stabilizer. The transplant psychiatry team is asked to opine on the patient’s candidacy.

Comment: Some 5–22% of patients may require a second liver transplant, most commonly for hepatic artery thrombosis or allograft failure.^{16,17,18} From a psychiatric perspective, mood disorders such as bipolar I or II may respond to, or even require, antipsychotic treatment during the course of illness, but more robust data seem to support the use of mood stabilizers, such as lithium, valproate, or lamotrigine, for maintenance treatment¹⁹. Although antipsychotics may have some advantages, such as ease of use, tolerability, and coverage of multiple symptoms (e.g., anxiety and insomnia), they also carry risk, such as weight gain, or development of involuntary movements (tardive dyskinesia).^{20,21} In this case, poor access to medical care in the patient’s vicinity may have contributed to the use of an antipsychotic over some mood stabilizers, which require more monitoring, prior to transplant. It was also poor access to medical care for the patient, specifically psychiatric, that may have led her to continue care under treatment by the transplant psychiatry team *de facto*. Typically, we try to make distinct our roles as either rendering opinion regarding patient candidacy, or treatment of patients in the transplant period. In reality, the lines may become often blurred²²; for instance, we might provide treatment recommendations as part of an evaluation for transplant candidacy. From an ethical standpoint, this fine line might be viewed as a question of beneficence: is it via ongoing treatment of the patient’s chronic psychiatric condition, or as an evaluator for life-saving retransplant? In this case, we asked another psychiatric colleague to evaluate the patient for her potential candidacy for second transplant, as we felt our treatment of the patient, as infrequent as it was, might bias us in consideration for relisting. By recusing ourselves for candidacy evaluation and continuing ongoing input regarding the treatment of her bipolar disorder, our aim was to optimize beneficence in as unbiased manner as possible.

Case 4: A 58-year-old single man with chronic hepatitis C and resultant hepatocellular carcinoma is being considered for liver transplant candidacy. The patient carries a diagnosis of schizophrenia, which has been stable over the last decade at least via treatment with clozapine. Previous to current treatment the patient was psychiatrically hospitalized frequently, with prominent paranoia, delusions, and disorganized thought process which robbed him of any semblance of fulfillment of the potential suggested prior to his psychiatric condition. It is suspected he may have contracted hepatitis C during his early 20s, when he used intravenous drugs for a brief time, coinciding with onset of his psychosis.

He has since lived a sober lifestyle, and has been consistent with all aspects of his care, including adherence with all medications, blood monitoring required for the clozapine, and associated weekly group treatments. He otherwise leads an isolated existence, living semi-independently in supported housing for the chronically mentally ill. He visits with his case manager as required, and occasionally sees his lone surviving family member, his sister. Upon evaluation, the patient is free of any prominent hallucinations or delusions; however, his mental status is strikingly odd, with flat affect, intermittent uncued laughter, poor eye contact, and very limited, concrete responses to questions.

Comment: Once the most common underlying disease necessitating liver transplant, hepatitis C has been dramatically reduced as the causative factor among the ranks of patients awaiting a new liver, thanks to the advent of protease inhibitors that are highly effective at eliminating the virus.²³ Nevertheless, hepatocellular cancer (HCC) may develop even in individuals successfully treated for hepatitis C, and given the high recurrence rate, once cancer is present, liver transplant remains the definitive treatment for HCC.²⁴ The issue at hand in the case above is: given the limited supply of donor liver organs, is it ethically permissible to consider a candidate with another debilitating disease deeply affecting his quality of life—in this case, schizophrenia? The patient's treatment for schizophrenia has ostensibly been optimized, at least from a pharmacologic perspective, as his current regimen of clozapine is widely regarded as superior to any other antipsychotic.²⁵ Nevertheless, curative treatment for chronic psychotic disorders such as schizophrenia remains elusive, and even those with the best available treatments will continue to experience some symptoms. In this patient's case, those residual symptoms consist not of the more well-known positive symptoms (hallucinations, delusions, etc.) but the more devastating negative symptoms, affecting interpersonal interaction, affect expression, and cognition. Negative symptoms in particular tend to evade pharmacologic intervention, and are thought to be the cause of more long-term disability.^{26,27} Moreover, despite the wide heterogeneity of disease and course, we might expect the patient's schizophrenia to progress further over time²⁸; dementia, another progressive neuropsychiatric condition without known cure to date, has been considered a relative, if not absolute, contraindication for transplant candidacy. But to deny this patient consideration for transplant based on his psychiatric condition alone would stand on shaky ethical ground. Consideration for candidacy involves the projected ability for the potential recipient to care for the donor organ; based on this patient's treatment history of his schizophrenia, he has already demonstrated consistent adherence with much that is required to maintain a transplanted graft organ—taking medications, obtaining phlebotomy for lab monitoring, and maintaining healthcare visits. His psychotic disorder may worsen over time, but generally not as rapidly as most dementias. His relatively limited existence may give pause to a candidacy selection committee, particularly as they keep other patients in mind—those with children, families, jobs, or other endeavors with a positive impact on others, who may also await liver transplant. But it would be ill-suited for this selection committee, or medicine in general, to mete out this sort of value judgment, being contrary to distributive justice, another pillar of medical ethics. Transplant candidacy for those with severe mental illness has been considered previously from an ethical standpoint, and the potential for psychiatric patients to be marginalized due to prejudice against them has been rightly pointed out; however, the solution offered, wherein psychiatric patients are considered separately from other candidates, potentially may further contribute to their marginalization²⁹.

Case 5: A 58-year-old man with end-stage liver disease due to alcoholic cirrhosis is admitted to the intensive care unit intubated in fulminant liver failure. The patient has multiple medical issues as a result of his liver illness, and transplant is urgently being considered, as perhaps the only reasonable medical means to survive from this hospital admission. His family, whose ethnicity (as is the patient's) is distinct from the majority of the treatment team, is found by the hospital staff to be hard to contact despite the urgency of the patient's condition. When the family finally arrives, there is immediate tension, with the medical team perceiving a hostile, accusatory stance by the family. Family members, in turn, do not trust the primary team. They are indignant regarding the team's inquiry into the patient's past, including his length of sobriety from alcohol, and demand that the patient be transferred to another medical facility. However, the hospitals which the family requests, all closer to their home, do not offer transplant as a treatment option, causing an impasse.

Comment: Based on prior work by the head of service at our institution, it has been the standard of care for transplant recipients to achieve a minimum of 6 months of sobriety to be considered a transplant candidate for alcohol related liver failure, as a shorter duration has been demonstrated to be the main risk factor in post-transplant relapse.³⁰ More recent work has suggested a less lengthys obriety window may still result in good recipient and graft organ survival in select cases where transplant candidacy is the result of index presentation to medical care, and highly reliable social support is available for the patient post-transplant.^{31,32} As clear-cut as the latter may seem, it is prone to opinion, interpretation, and bias as with any interpersonal exchange. Even if the patient in the above case were to have had a prolonged period of sobriety prior to this presentation, could he be considered for transplant candidacy, based on the toxic nature of the relationship developing between his family and his current treatment team? It is impossible for any patient to be a transplant candidate without some sort of social support, which is required to provide the near-constant home care required in the immediate postoperative period—but typically does much more, before and after the transplant. Transplant is not an endeavor to be journeyed upon unaccompanied; in those first crucial weeks after surgery, the day-to-day changes required in the antirejection medication regimen alone make a reliable support individual, typically a spouse or another family member, vital. That support person (may be a team of individuals) is the main conduit between transplant care team and patient, and without good relations on both sides, survival of both graft organ and recipient may suffer. Interfacing with medical personnel can be an art in itself—medicine has developed its own subculture, and those outside of it, including many patients, may feel lost, pushed around, or unheeded. In turn, the transplant team is often sensitive to the responsibility it carries, not just to the patients they treat, but to the donors and their families—typically unseen, but heralded for their life-saving gift at a time of loss—as well as the legion of other candidates not so fortunate, dying before they get their second chance at life. Thus, both support individuals and transplant team may face potential obstacles to smooth relations—and this may come even before considering factors of race and ethnicity.

It is difficult to contemplate distributive justice, from a medical ethics standpoint, without consideration of social justice, where the inequalities due to race and ethnicity are addressed from the potential biases inherent in institutions, including medicine. Perhaps no area such as transplant, or any other life-saving measure, deserves such scrutiny, and assurance of fairness—equal access to transplant may be one practical measure of a particular society's level of true equality for its citizens. The illustrative case deliberately did not include specifics regarding race or ethnicity, so that it might be used to consider any minority group that may be subject to bias; in practice, however, it behooves the medical treatment team to be aware of the specific barriers a particular individual patient may face in light of their race, ethnicity, or other non-majority identity, and ideally provide specific direction to overcome them. Much work has been done,^{33,34,35} and promises to continue,³⁶ from a population-based perspective regarding potential inequalities in transplant, but ultimately distributive and ethical justice in medicine is upheld one patient at a time.

A high bar—of conduct, care, and collaboration—must be set for all post-transplant, including the treatment team, care support individuals, and patients—we owe it to the donors, other candidates, and the recipient patient as well. But the bar must be within reach of all equally, as both distributive and social justice demands. Psychiatry is in no way the sole purveyor of justice within the medical field—in fact, it is ultimately all of medicine's goal to bridge gaps, to overcome disparities and barriers, and make available care for all. In this case, our transplant psychiatry service was consulted to join the hospital ethics team, to speak with the family regarding options available to the patient, and provide guidance on the most ethically sound next clinical steps. It is not clear exactly what made things work—their patience, empathy, communication skills, the diversity of their team, or simply for the family to hear information in a different manner, from a different source—but the ethics team was able to help the family come to a workable solution, to transfer the patient to another transplant facility within the area, so that the patient might be considered for candidacy there. Perhaps just as importantly, the family was able to express and consider some of the emotions surrounding their family member's life-or-death condition, which they noted was an ongoing process. We too, in the field of transplant, must continue our ongoing journey toward ethically sound justice within our purview.

Notes

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