Liver Transplant—Psychiatric and Psychosocial Aspects

Sandeep Grover, Siddharth Sarkar

Department of Psychiatry, Postgraduate Institute of Medical Education & Research, Chandigarh 160012, India

Liver transplantation is a life saving surgical procedure that is associated with improved longevity and enhanced quality of life. The number of successful liver transplants is growing worldwide. The procedure requires a dedicated and trained team of experts. A psychiatrist plays an important role in such a team. Psychiatric and psychosocial assessment is considered imperative to evaluate the candidate's suitability as a transplant recipient. Many psychiatric disorders may lead to the need for liver transplant, and if kept unchecked can adversely affect outcomes. Psychiatric problems arising in the post-transplant period may also require intervention of the psychiatrist. The donor too needs to be evaluated adequately to assess for psychological fitness for the procedure. This article provides broad overview of the various psychiatric and psychosocial issues pertaining to liver transplantation. (J Clin Exp Hepatol 2012;2:382–392)

After the advent of potent immunosuppressants, the number of solid organ transplants has increased substantially.[1] The organs that are transplanted from one person to another include kidneys, liver, heart, lungs, and pancreas among others. The field of transplant medicine has emerged as a growing specialty and has seen many innovative procedures, surgical techniques, and improved aftercare measures.[2] Encouraging results have been obtained, with better patient outcomes and longevity.

Since the conduct of first successful liver transplant in 1967, the number of liver transplants has grown steadily over the decades. It is now being conducted all over the world in increasing counts. Although around 6000 liver transplants are conducted in the United States in a year,[3] the number of cases requiring transplant on the waiting list are far more than the number of procedures done in a year. With the live donor liver transplantation, the numbers of liver transplantations conducted has increased significantly.

The procedure of liver transplantation is carried out by a team of experts and specialists, who endeavor to improve outcomes by playing a role before, during and after the surgery. The psychiatrist/mental health professional can have a very important role to play in such a team. There can be mental health issues that lead to the liver transplant in the first place, for example, liver damage due to alcohol dependence or a suicidal attempt in which person intentionally takes overdose of acetaminophen leading to hepatic failure. Once the decision for liver transplant is taken, waiting for transplant may lead to anxieties about survival and availability of the organ.[4] Patients may be apprehensive about asking potential donors for help in case of live donor transplantation.[5] The transplant procedure as well the conditions leading to it can be quite stressful for the patients and may have psychiatric and psychosocial implications. Post-transplant, patients require regular compliance to lifelong immunosuppressants and modification in lifestyle, including abstinence from alcohol. All these factors challenge the coping of the patients, and increase the likelihood of emergence of psychological symptoms. The psychiatrist/mental health professional with expertise in dealing with such problems, would be placed at a unique position to contribute to enhanced patient care, and improved outcomes. This review provides a broad overview of the various psychiatric and psychosocial issues pertaining to liver transplantation.

PSYCHIATRIC DISORDERS IN PRE-TRANSPLANT PHASE

Patients with liver failure requiring liver transplantation can have various psychological and psychiatric problems. Timely identification and treatment of these can lead to improvement in condition of the patient, thereby optimizing the pre-operative fitness. An important aspect of evaluation is the proper documentation of the same. It not only serves the purpose of record keeping, but helps in clearer decision-making regarding management of psychiatric condition and better communication with other members of the treatment team. It is in general suggested that treatment recommendations need to be made, taking into consideration all the pertinent aspects of a particular patient.

The most commonly encountered psychological problems include alcohol use disorders, opioid use disorders, anxiety disorders and depressive disorders. Alcohol liver

Keywords: psychiatry, psychosocial, liver transplant
Received: 22.5.2012; *Accepted:* 17.8.2012
Address for correspondence: Dr. Sandeep Grover, Assistant Professor, Department of Psychiatry, Postgraduate Institute of Medical Education & Research, Chandigarh 160012, India. Tel.: +91 172 2756807 (O); fax: +91 172 2744401, +91 172 2745078
E-mail: drsandeepg2002@yahoo.com
http://dx.doi.org/10.1016/j.jceh.2012.08.003

disease (ALD) is one of the commonest reasons for undergoing liver transplantation.[6,7] In most of such cases of ALD, diagnosis of alcohol dependence is tenable.[8] Debate has continued as to whether and when ALD patients should be considered for transplantation. Some argue from a moralistic standpoint that since alcohol had been consumed by a person willfully leading to complications,[9] so scarce grafts should not be expended on alcohol users. Others assert that there is no difference in survival of ALD transplant cases as compared to others, and a majority of patients with ALD do abstain from alcohol after transplantation.[10–12] Hence these patients should be considered for transplantation. Currently most centers require some duration of abstinence from alcohol before consideration for transplantation.[13] The requisite duration varies from center to center. It has been seen that longer abstinence prior to transplantation reduces the chances of relapse after the transplant.[14,15] However, other studies have shown that early transplant, even during the acute alcoholic hepatitis phase, is also associated with greater survival benefit over 2 years.[16] Interestingly, early transplantation has been found as a protective factor against relapse to alcohol when compared to cirrhotic patients on wait list.[17] Thus, deserving ALD patients should be offered transplantation.

Apart from pre-transplant abstinence, many other factors have been assessed as predictors of relapse to alcohol use post-transplant. These include a family history of alcohol use,[18,19] personality disorders[20,21] and poly-substance abuse.[18,22] Another important aspect is presence of psychiatric comorbidity in patients with ALD undergoing liver transplant. Studies have shown that presence of antisocial behavior and eating disorder increases the chances of relapse in the post-operative phase.[20] In a review of literature, it was found that social stability, older age, good compliance with medical care, absence of repeated alcohol treatment failures, absence of alcohol problems among first-degree relatives, absence of current polydrug misuse, and lack of co-existing severe mental disorder were associated with longer abstinence in the post-operative period.[23] Duration of pre-operative abstinence appears to be a poor predictor of abstinence despite extensive research and wide usage.[23] Intravenous drug use also has an important relationship with need for liver transplantation. It is an important risk factor for contracting Hepatitis C, which is among commonest reasons for liver transplantation. Hence drug dependence, especially of injectable drugs like opioids and cocaine, needs to be carefully screened. One study suggests that outcome of intravenous drug users with Hepatitis C related liver transplantation is not substantially different from non-drug users.[24] Poly-substance use disorder however, has been seen to adversely affect the outcome in ALD. In a study of liver transplant patients it was seen that approximately one third of the transplanted poly-substance users relapsed to substance use.[25]

Opioid users have been traditionally considered unsuitable for liver transplantation. In a mailed survey of transplant programs,[26] it was noted that approximately only half of the programs accepted patients on methadone maintenance. Of those, a significant proportion required that the methadone be tapered off before the transplant. However, some authors have argued against the same.[27] Studies done in patients on methadone maintenance treatment (MMT) in general show that tapering off of MMT results in relapse to illicit opiate use in 80% of patients.[28] Hence, asking the patients to taper off methadone at the time when they are dealing with the stress and pain of end-stage liver disease and are facing liver transplant may increase the risk of relapse. Further, if a patient relapses, he or she would be removed from the list of those eligible for transplantation. Studies have also shown that in general there is no difference in the MMT liver transplant recipients and general transplant population with regards to adherence to immunosuppressive medications and overall graft survival rates.[26,29,30] Hence such patients should be evaluated on a case to case basis and methadone can be safely continued in the post-transplant period in the usual doses. Those patients who are on stable adequate doses of methadone, follow other measures of MMT program and have excellent social support should be considered for liver transplant.

Many studies have been conducted to assess depressive symptoms in patients awaiting liver transplantation.[31–40] The sample sizes of such studies have ranged from 20 to 247.[31–40] Various instruments have been used to measure and diagnose depression including self-rating scales like Beck Depression Inventory; clinician rated scale like Hamilton Depression Rating Scale and structured interviews with professionals. The rates of depression have varied from 4.5% [31] to 64%.[33] The different measures for assessing depression and different methodologies of assessing (self versus clinician rated) can account for some of the variance in prevalence of depression. In a comparatively large study by Bianchi et al[35] with relatively rigorous methodology, significant depressive symptoms were present in approximately 57% of the sample using Beck Depression Inventory. Attempt have also been made to differentiate the rates of depression relating to different etiologies of cirrhosis, with some studies reporting higher, whereas others reporting lower or no difference in the rates of depression in patients with viral etiology for cirrhosis compared to other etiologies.[27,28,31] Identification of depression in the pre-transplant phase is important, because there is some evidence to suggest that presence of depression in the pre-transplant period is associated with non-adherence with treatment.[41]

Studies have also delved into the occurrence of anxiety disorders and adjustment disorder in patients awaiting liver transplantation. Different methods have been used to measure anxiety like Beck Anxiety Inventory, Hospital

Anxiety Depression Scale, and structured clinical interviews. The results show the prevalence of anxiety symptoms or anxiety disorders varies between 20 and 50% in the patients awaiting transplantation.[31,32,37–39,42,43] Among the various anxiety disorders, presence of adjustment disorders[31,37,38] and obsessive symptoms[42] have been documented in a significant proportion of patients. A study in which domains of anxiety and depression were combined, reported a diagnosis of adjustment disorder or depression in upto 36% of the patients awaiting liver transplantation.[44]

Personality characteristics and coping abilities have been evaluated in patients waiting to undergo liver transplant. It has been seen that patients frequently have maladaptive coping styles with poor fighting spirit, anxious preoccupations, hopelessness, negation and fatalism being found frequently.[45] Negative coping styles that include acceptance-resignation strategy were associated with a worse perception of physical functioning, general and mental health.[46] Others have reported psychological regressive functioning (high control and dependency on medical staff, submissiveness) in patients waiting for liver transplantation, which can be interpreted as defensive responses to upcoming transplant.[47]

Another common psychiatric entity which has been reported in pre-transplant patients is delirium. It is reported in up to half of patients prior to liver transplantation.[31,48,49] This may be ascribed to hepatic encephalopathy and other associated medical factors like electrolyte imbalances and infections. It is important to identify delirium as the presence of this condition may impair the ability of the patient to fully comprehend the implications of the transplant and its related commitments.

Concern has been raised about whether psychotic disorders should be considered a contraindication to liver transplantation.[50] There have been instances where transplantation has been performed successfully in patients with schizophrenia and other psychoses.[51,52] The common problems encountered before and after the transplant in psychotic patients include non-compliance to psychotropic and immunosuppressant medications, risk of suicide attempts and recurrence of the psychotic symptoms.[52] Being homeless or living alone is associated with higher rates of non-compliance to medications in these patients. Hence, it is recommended that due consideration should be given to control the psychotic symptoms in the pre-transplant phase and the symptoms should be closely monitored in the post-transplant period.

PRE-TRANSPLANT ASSESSMENT

Pre-transplant evaluation is used to identify psychiatric illnesses and psychological problems in the patients,[53,54] and provides an opportunity to intervene and manage them effectively. This evaluation is a part of the preparatory stage for consideration of liver transplantation. It must be remembered that evaluation for transplant may be required on more than one occasion as there may be a delay in obtaining graft and attaining medical fitness for the surgery. Further, while carrying out the assessment, information must be obtained from all possible sources.

Certain cases, for example, those with acetaminophen toxicity will require urgent psychiatric evaluation. This situation may be complicated by patient being on mechanical ventilation, which compromises detailed psychiatric evaluation of patient. In such situations, information should be collected from other sources including that from caregivers and family members. In many cases, the decision for considering transplant is determined on the basis of the history. In general many transplant teams are more comfortable in listing a patient when the overdose appears to be an outcome of an isolated impulsive act precipitated by a stressful life event, rather than those who have recurrent pattern of self-harming behavior arising due to psychiatric disorders like alcohol dependence, personality disorders or mood disorder.[55]

PSYCHIATRIC EVALUATION

Identification and management of psychiatric problems in the pre-transplant phase is very important because these have a bearing on the post-transplant outcome. It has been shown that quality of life of candidates waiting for liver transplant is also influenced by psychiatric disorders. In a study which evaluated the quality of life of pre-transplant patients, it was seen that physical and mental wellbeing in liver transplant candidates were influenced far more by psychiatric factors such as depression and coping strategies than by clinical and sociodemographic factors.[38] Hence, identification and management of psychiatric disorders is of paramount importance to improve the outcome of patients waiting for the transplant and also in the post-transplant phase.

The protocol for assessment varies from center to center. It has been suggested that active psychiatric illness is a modifiable risk factor for poor outcome in transplant recipients.[56] Hence a comprehensive assessment is necessary.

A group of assessment measures encompassing a wide variety of functions can be utilized to obtain a comprehensive understanding of the patient. The assessment protocol can use a structured diagnostic instrument for psychiatric diagnosis,[57] instruments to assess depression, anxiety and delirium,[58–60] a structured personality assessment,[61] coping inventories,[62] neuropsychological batteries,[63] and others as deemed necessary. It has been seen that structured interviews lead to better accuracy of psychiatric diagnosis as compared to unstructured traditional diagnostic assessment.[64] The presence of psychiatric disorders can

be evaluated by the initial use of screening questionnaires followed by detailed psychiatric evaluation. Various screening questionnaires include generic instruments like General Health Questionnaire (GHQ)[65] or disorder specific questionnaires like Primary Care Evaluation of Mental Disorders (PRIME-MD)-Patient Health Questionnaire (PHQ).[66] These screeners can be followed by detailed relevant self-rated or clinician-rated instruments. GHQ was originally developed as a 60-item questionnaire as a unitary screening measure for psychological problems. Now the 30-, 28- and 12-item versions are in vogue. The 12-item version is a very popular screening measure. Each item is noted on a 2—point scale (better than usual or same as usual is rated as 0, and less than usual or much less than usual is rated as 1). PRIME-MD PHQ is a self-report screening instrument which can be used to screen/diagnose common mental disorders. It includes 8 diagnostic categories, viz. major depressive disorder, panic disorder, other anxiety disorder, bulimia nervosa and other sub threshold disorders such as other depressive disorders, probable alcohol abuse or dependence, somatoform disorder and binge eating disorders. There is high degree of agreement on the presence of psychiatric illness as assessed by PHQ and physicians.

Patients undergoing liver transplantation pose difficulty in diagnosis of depression due to the emergence of somatic symptoms from the underlying medical illnesses and the concomitant medications. Hence alternative approaches to ascertain depression can be utilized as has been done for other medically ill patients.[67,68] Certain items from the substitutive criteria like 'brooding, self-pity or pessimism' and 'cannot be cheered up, doesn't smile, no response to good news or funny situations' may be useful for detection of mild and severe depression, respectively, as has been found for cancer patients.[69] Beck Depression Inventory[58] which focuses on the cognitive aspects of depression may be a better suited instrument for assessment of depression in liver transplant candidates. It is a 21-item self-report instrument for measuring the presence and severity of depressive symptoms. It is one of the most widely used instruments for measuring the severity of depression. It can also be used to monitor change in depressive symptoms over time and provide an objective measure for judging improvement.

Other important psychiatric aspects to be considered are antisocial and borderline personality features, history of assault, positive psychotic symptoms such as hallucinations and delusions.[53]

PSYCHOSOCIAL ASSESSMENT

Besides core psychiatric disorders, there can be many psychosocial issues which can influence the outcome of liver transplant. Hence, a detailed and comprehensive psychosocial evaluation is imperative in patients undergoing liver transplantation. This would be helpful in understanding the circumstances and the profile of the patient better, allowing requisite changes to be incorporated in the management. In this evaluation, information needs to be gathered from as many sources as possible. The patient's own history, significant other's account, medical records, insurance records, nursing staff's inputs and other sources may give valuable information. At times patients may be motivated to conceal certain information so that they are not excluded from the transplant list. This may happen especially in cases of alcohol use disorders where the patient may minimize or deny recent use of alcohol so that they are considered appropriate candidates for transplant.[70]

The salient features of the psychiatric and psychosocial evaluation are highlighted in Table 1. The evaluation of the patient typically involves determining the coping skills and other psychological attributes of the patient, gauging the social situation, assessing the patient's capacity to give informed consent, and ascertaining the likely adherence to post-transplant care. Information should be specifically recorded about alcohol and substance use as these often create the need for the transplant, and relapsing to such behavior may worsen the outcome.[23]

Considering the importance of psychological issues, different instruments have been designed to carry out

Table 1 Psychosocial evaluation of the patient.

Assessment of psychological attributes of the patient
Coping styles
Grief
Hopelessness
Adaptation to illness
Illness behavior
Commonly applied defense mechanisms
Motivation for surgery
Personality
Past treatment compliance
Quality of life
Evaluation of the social supports
Availability of an identified caregiver
Availability of alternative person(s) in case primary caregiver is not available on a particular day
Assess for the financial condition and supports
Availability of adequate finances/ insurance cover for the transplant procedure
Ability to afford for lifelong immunosuppressant medications
Assess ability to understand the transplant procedure and the associated risks and liabilities, to put the expected benefits in the right perspective, give informed consent
Assess the likely adherence to the treatment

comprehensive psychosocial assessment of patients to undergo liver transplantation. The Transplant Evaluation Rating Scale (TERS)[71] classifies patients' level of adjustment in ten aspects of psychosocial functioning. The scale shows a good inter-rater reliability and has been evaluated in liver transplant recipients. Psychosocial Assessment of Candidates for Transplantation (PACT) is another instrument that has been used in this population.[58] PACT has eight subscales, each rated on a 5-point scale, and an initial and final rating independently based on the rater's overall impressions of the candidate's acceptability for transplant. Recently, Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT) has been evaluated in transplant candidates.[72] The instrument shows good inter-rater reliability, and good correlation with psychosocial outcome. Use of any one or combination of these instruments can help in deciding transplantation candidacy.

The liver transplant is a stressful procedure. The patient requires emotional support, good nursing care, regular follow up, proper medication adherence and monitoring subsequent to the transplantation. These are facilitated by the presence of a support figure. Social supports are required for pragmatic reasons to ensure patients' psychological and medical well being. Hence it is useful to have an identified caregiver who would co-ordinate the care and act on behalf of the patient when in need. He or she may be needed to decide on behalf of the patient if the latter becomes incapacitated. Alternate supports also need to be enlisted for possible situations when the primary caregiver is unavailable to provide care, or takes a vacation. The caregiving process has its own stress and emotional well being of such caregivers also need to be attended to.[73,74]

An important aspect of assessment is evaluation of competence to give informed consent. It needs to be ascertained whether the patient is in a condition to fully comprehend the implications of his or her decision. The transplant requires a lifetime commitment and major changes in lifestyle. It is useful to unambiguously provide as much information as possible, before a decision is made.[75,76] In case patient is not deemed to have capacity to give such consent, then the onus falls on the identified legal guardian to make such a decision on his/her behalf. The issue of confidentiality should be treaded carefully. The patient may disclose confidential information to the mental health professional which may have implications in the overall management. For example history of intravenous drug use concealed from others, fearing stigma or rejection from candidacy. It may be prudent to convey to the patient beforehand that requisite information would be shared with the multidisciplinary transplant team members for his or her benefit.

At times, emergency evaluation may be necessary especially in cases of acute hepatic failure.[77] Therein limited time may be available to conduct detailed assessments. Moreover, patient's condition may not permit a clinical interview. It may be practical to gather as much information as possible from the collateral sources to generate an impression of the patient's psychological condition. Thus, assessment is expedited and so that a life saving procedure can be conducted in due time.

PSYCHIATRIC ISSUES AS CONTRAINDICATIONS FOR LIVER TRANSPLANT

It is important to remember that some of the psychiatric aspects as depicted in Table 2 are considered as relative contraindications for liver transplant. These conditions must be interpreted with caution as mere presence of these does not preclude a patient from being a recipient.

PSYCHIATRIC PROBLEMS IN THE POST-TRANSPLANT PERIOD

In the immediate post-transplant period, many psychiatric problems can arise which may necessitate the involvement of the psychiatrist/mental health professional. Delirium (also referred to as encephalopathy) is reported to be the most common neuropsychiatric problem after the transplant surgery.[78–80] It is characterized by confusion, disorientation, fluctuation in consciousness and agitation, and poses as a management difficulty in the intensive care unit. Development of encephalopathy has been associated with higher rates of mortality.[80] The causes of delirium can be varied in a patient of liver transplantation and may include concurrent brain pathological processes, e.g. infection or bleed; effects of vasoconstriction secondary to immunosuppressive medications (especially cyclosporine and Tacrolimus); and central nervous system pharmacodynamic effects of the immunosuppressive medications.[81] Evaluation of delirium during this period of time must include careful medical examination of the patient and a review of the medications and laboratory studies. Neuroimaging, EEG recording, and lumbar puncture can also provide valuable information in evaluating the cause of delirium.[82] Delirium can be managed with low dose antipsychotics (oral and injectable) and behavioral interventions, along with addressing the underlying cause.

Table 2 Psychiatric and psychosocial contraindications of liver transplantation.

Severe personality disorders
Active substance use
Active psychosis
Severe neuro-cognitive disorders
Suicidality
Absent or inadequate psychosocial supports
Demonstrated poor adherence
Factitious disorder

Apart from delirium, development of catatonia has been reported in the post-operative period.[83–85] Medical complications of the transplant can also present as other psychiatric disorders. Hepatic artery thrombosis has been found to be associated with development of psychosis.[86] Hence a careful assessment of the symptoms, and proper psychiatric examination is warranted.

Many psychiatric disorders have been seen to be present subsequent to liver transplantation. The rates of depression have ranged from 5% to 46%.[87,88] In a follow up series, Fukunishi et al[89] using interviews by trained professionals in the post-transplant period found psychiatric illnesses to be present in 22 out of 41 (54%) of adult recipients within 3 months post-transplant. The diagnoses included delirium in 7 patients, depression in 5, dysthymia in 4, adjustment disorder in 3, brief psychosis, PTSD and substance related disorder in one patient each. Over longer follow up of 1 and 3 years, lesser numbers of patients had diagnosable psychiatric disorders (7% and 2% respectively).[78] Rothenhäusler et al[87] studied 75 liver transplant patients post-operatively for psychiatric disorders and found at least one disorder in 17 patients (22.7% of sample). The authors found full PTSD in 2 patients, full PTSD and depression in 2 patients and partial PTSD (having symptoms of PTSD, but not meeting full criteria) and depression in one patient, and partial PTSD in 12 patients. Chiu et al[90] reported that upto 70% of the patients had psychiatric disorders in the post-transplant period and anxiety, depression and delirium were the major reasons for referral to a psychiatrist/mental health professional. Pérez-San-Gregorio et al[91] noted that depressive symptoms as measured by HADS were more common in the ICU post-transplant, while anxiety was present in the post discharge phase. High levels of post-transplant anxiety resulted in reduced functioning in multiple life domains.[91] Russell et al[88] showed that the rates of anxiety and depression decrease significantly when compared to the pre-transplant rates.

A '*paradoxical psychiatric syndrome*' has been described in recipients of liver transplantation.[89] It has been termed paradoxical as it develops despite successful transplantation. It develops late after the transplantation and is characterized by recipients having strong guilt feelings toward their donors, not being able to verbalize their inner feelings, and using avoidant coping behaviors to suppress their conflicts. The *'paradoxical psychiatric syndrome'* has been shown to be associated with pre-transplant alexithymia and abnormal projective drawing in the recipients.[92]

MANAGEMENT OF PSYCHIATRIC DISORDERS AND OTHER PSYCHOSOCIAL ISSUES

The psychiatrist/mental health professional have an important role in management of psychiatric disorders detected before and after the transplantation. Besides this the psychiatrist/mental health professional have an important multifaceted role in the continuum of care of transplant recipients (as mentioned in Table 3).

Many of the psychiatric illnesses can be treated with effective pharmacotherapeutic and psychotherapeutic interventions. Particular consideration needs to be given to pharmacological interactions as these patients may be receiving a variety of medications. Pharmacological options primarily include antipsychotics for management of delirium and psychosis, antidepressants for anxiety and depression, and benzodiazepines for anxiety and sleep problems. When needed mood stabilizers, anticraving agents and deterrent agents can be given. Attention needs to be paid toward possible drug interactions, especially with the immunosuppressants that are prescribed to avoid graft rejection. While reviewing the drugs it is important to look for not only the prescription drugs, but attention also must be paid to over the counter medications. Tacrolimus may potentiate the QTc prolongation with antipsychotics, especially first generation antipsychotics like haloperidol. It can also potentiate nephrotoxicity when co-administered with lithium. Systemic steroids can increase the chances of seizures with bupropion. Carbamazepine may decrease the blood levels of cyclosporine due to induction of hepatic metabolism.[93,94]

In patients with history of alcohol use and ALD, relapse to alcohol taking behaviors has been considered as a major challenge. The relapse rates have been found to vary from about 10 to 30%.[14,18,19,95,96] The predictors of relapse to harmful use of alcohol include shorter duration of abstinence, presence of psychiatric comorbidities, younger age, and high scores on scales assessing risk of relapse.[95–97] Different trajectories of alcohol use pattern after transplantation has been reported.[12] Preventing lapse and relapse to alcohol use is of significant importance. Even in cases of lapse or relapse, immediate and effective treatment interventions can delay and avert harms of alcohol use.

Table 3 Role of the psychiatrist in the management of the patients of liver transplant.

Appropriate treatment of the pre-existing substance use disorders and other psychiatric disorders
Consideration toward possible interaction and side effects with pharmacological agents
Assess for emergence of psychiatric symptoms, institute relevant management measures in case they arise
Conduct psychotherapy when incorporated in management plan
Enhance adherence to treatment
Communicate the expectations of the treatment team to the patient and give patient's feedback to the treatment team
Engage in support groups if available
Develop and monitor occupational and social rehabilitation plan

A major issue in liver transplant recipient is long term adherence to treatment. Poor adherence not only manifests as failure to take prescribed immunosuppressants on a regular basis, but also as missed appointments to the physicians, failure to get required laboratory tests done, and failure to conform to lifestyle changes like avoidance of alcohol and smoking.[98] The problem of non-adherence has been found to be present in both children and adult recepients.[99,100] There is no single intervention demonstrated to reliably improve adherence, and it appears that a multifaceted approach involving reminders, enlisting co-operation of significant others, and motivation enhancement may be of use.[89]

Undergoing liver transplantation may be associated with some improvement in health related quality of life.[101,102] There is improvement in quality of life as compared to pre-transplant period, but quality of life remains poor in most domains when compared to general population.[102] In a long term follow up study it has been shown that the improvement in various domains may not be sustained over time, and may differ with etiology of liver failure.[103] The occupational and social rehabilitation plan needs to consider these findings. The patient may be able to regain previous activities and vocations. However, not all occupations would be sustainable for transplant recipient, due to the requirement of regular and timely medications and avoidance of sources of infection. Detailed plan of gradual reinstatement of occupational and social roles can be worked out in consultation with the patient.

Besides all the above, a psychiatrist due to his or her expertise is at a better position to communicate the concerns of the patient to the treating team and vice versa. He or she has the opportunity to allay the undue anxieties of the patients and answer queries and doubts. Structured psychotherapy can be done by the psychiatrist when deemed required. This may be especially helpful in abstinence from alcohol and other substances, either pre-transplant or post-transplant.[104]

DONOR RELATED ISSUES

With time, the number of living donors for liver transplant has gradually risen. They are usually a family member of the patient, often a spouse or a parent.[75] Most donors consider organ donation as a positive experience and would donate again if needed.[105–107] In a comparison of actual and potential donors, it was seen that actual donors have a higher self-esteem,[108] reflecting that donor felt a sense of purpose.

The psychosocial evaluation of the donor may be grounds for disqualification from surgery in many cases and can range from 8 to 20%.[109–111] Careful assessment of the donor would help in reducing the effects of coercion leading to donate, and could possibly reduce the chances of dissatisfaction among the donors.

The psychosocial evaluation of these donors is as important as that of the recipient. The various aspects which need to be covered are detailed in Table 4. Information needs to be gathered about any psychiatric illness in the donors. It has been seen that rates of pre-transplant psychiatric disorders correspond to mental health of the donors after the procedure.[112] Nonetheless, having a psychiatric illness of the donor should not be considered a contraindication for organ donation. It is beneficial to institute treatment and optimize mental health of the donor prior to the surgery. Psychiatric symptoms can also arise post-operatively as a consequence of unrealistic expectations or peri-operative complications.[113] In a large sample of donors with a median follow up of 6 months,[114] the occurrence of post-operative psychiatric complications in donors was 4.1% (16 out of 392 donors). The post-operative illnesses included depression (12 patients), anxiety (2 patients), substance abuse (2 patients), bipolar disorder, accidental overdose, insomnia, crying episodes and worsening of obsessive-compulsive disorder (1 patient each).

It is important to focus on the informed consent of the donors as they themselves are at significant surgical risks during the procedure. It has been seen that though clinicians explain about risks and benefits, donors report unmet information needs. There are knowledge gaps regarding risks and unanticipated complications.[102] At times donors are pressured to give informed consent or may have some concealed internal motive for organ donation.[115,116] One author suggests that decisions about donation were reached before the 'informed consent process' was conducted in propriety.[117] The process of giving adequate information to the donors and allowing them to choose a course of action is of vital importance.

It is necessary to guard donor against coercion, but situations may not be fully clear at times. There may be entrenched dynamics in the family system which may not be apparent easily. The 'black sheep syndrome' in such a situation refers to disrespected family member attempting to gain appreciation by donating the organ.[118] Moreover, there may be a combination of elements of coercion as well as sense of genuine affection toward recipient, and the role of each needs to be teased out. It has been seen

Table 4 Psycho-social evaluation of donors.

Evaluation for psychiatric illnesses, past and present
Assessment of psychological strengths and weaknesses
Enquiry about understanding of the transplant procedure and it's implications
Assessment of capacity for informed consent
Relationship with the recipient and closeness
Evidence of coercion or financial motivation for being a donor
Availability of social supports for peri-operative period, especially if the donor is the identified caregiver for longer term

that donors who were conflicted about the decision and who were pressurized had more anxiety and depression, and a poorer quality of life post-transplant.[105] It would be valuable to understand the concerns and feelings of the patient toward the recipient, as well as the closeness, to make a confident impression. Post-transplant concern of the donor about the organ has been described, especially when the recipient had been ill.[119] Known as the 'Siamese twin effect', such an observation was not robustly found in a study from Japan.[120] The donor not only needs psychological support pre-operatively, but also post procedure. Significant others as well as therapists may help in providing such a support.

CONCLUSIONS

The numbers of liver transplantation bases has been steadily rising over time, and there is increasing emphasis on psychosocial assessment in order to improve patient outcomes. Such an assessment should be multidimensional covering past and present psychiatric and substance use disorders, psychological strengths and weaknesses, ability to give informed consent, availability of financial and social supports, and so on. The aim of this assessment is a better understanding of the patient. The assessment of donors also needs to be emphasized. All the liver transplant units should have a psychiatrist/mental health professional as a part of the transplant team who should work with the patient, the donor and the family of both to address the psychiatric and psychosocial issues arising in the context of liver transplant.

FUNDING

None.

CONFLICTS OF INTEREST

All authors have none to declare.

REFERENCES

1. DiMartini AF, Dew MA, Trzepacz PT. Organ transplantation. In: Levenson JL, ed. *The American Psychiatric Publishing Textbook of Psychosomatic Medicine*. Washington DC: American Psychiatric Publishing; 2005:675–700.
2. Multidisciplinary Heidelberg Transplant Symposium. *Innovations in Transplantation Medicine: Proceedings of the Annual Multidisciplinary Heidelberg Transplant Symposium, Villa Bosch, Heidelberg*; October 2007.
3. Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR). *OPTN/SRTR 2010 Annual Data Report*. Rockville, MD: Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation; 2011.
4. Engle D. Psychosocial aspects of the organ transplant experience: what has been established and what we need for the future. *J Clin Psychol*. 2001;57(4):521–549.
5. Lipkin GB, Cohen RG. *Effective Approaches to Patients' Behavior: A Guide Book for Health Care Professionals, Patients, and Their Caregivers*. Springer; 1998.
6. Burra P, Senzolo M, Adam R, et al. Liver transplantation for alcoholic liver disease in Europe: a study from the ELTR (European Liver Transplant Registry). *Am J Transplant*. 2010;10:138–148.
7. Lucey MR. Liver transplantation in patients with alcoholic liver disease. *Liver Transpl*. 2011;17:751–759.
8. DiMartini A, Dew MA, Javed L, Fitzgerald MG, Jain A, Day N. Pretransplant psychiatric and medical comorbidity of alcoholic liver disease patients who received liver transplant. *Psychosomatics*. 2004;45:517–523.
9. Burra P, Lucey MR. Liver transplantation in alcoholic patients. *Transpl Int*. 2005;18:491–498.
10. Mackie J, Groves K, Hoyle A, et al. Orthotopic liver transplantation for alcoholic liver disease: a retrospective analysis of survival, recidivism, and risk factors predisposing to recidivism. *Liver Transpl*. 2001;7:418–427.
11. Lim JK, Keeffe EB. Liver transplantation for alcoholic liver disease: current concepts and length of sobriety. *Liver Transpl*. 2004;10(suppl 2):S31–S38.
12. DiMartini A, Dew MA, Day N, et al. Trajectories of alcohol consumption following liver transplantation. *Am J Transplant*. 2010;10:2305–2312.
13. Snyder SL, Drooker M, Strain JJ. A survey estimate of academic liver transplant teams' selection practices for alcohol-dependent applicants. *Psychosomatics*. 1996;37:432–437.
14. Gedaly R, McHugh PP, Johnston TD, et al. Predictors of relapse to alcohol and illicit drugs after liver transplantation for alcoholic liver disease. *Transplantation*. 2008;86:1090–1095.
15. Tandon P, Goodman KJ, Ma MM, et al. A shorter duration of pretransplant abstinence predicts problem drinking after liver transplantation. *Am J Gastroenterol*. 2009;104:1700–1706.
16. Mathurin P, Moreno C, Samuel D, et al. Early liver transplantation for severe alcoholic hepatitis. *N Engl J Med*. 2011;365:1790–1800.
17. Di Martino V, Sheppard F, Vanlemmens C. Early liver transplantation for severe alcoholic hepatitis. *N Engl J Med*. 2012;366:478–479.
18. DiMartini A, Day N, Dew MA, et al. Alcohol use following liver transplantation: a comparison of follow-up methods. *Psychosomatics*. 2001;42:55–62.
19. Jauhar S, Talwalkar JA, Schneekloth T, Jowsey S, Wiesner RH, Menon KVN. Analysis of factors that predict alcohol relapse following liver transplantation. *Liver Transpl*. 2004;10:408–411.
20. Coffman KL, Hoffman A, Sher L, Rojter S, Vierling J, Makowka L. Treatment of the postoperative alcoholic liver transplant recipient with other addictions. *Liver Transpl Surg*. 1997;3:322–327.
21. Gish RG, Lee A, Brooks L, Leung J, Lau JY, Moore 2nd DH. Long-term follow-up of patients diagnosed with alcohol dependence or alcohol abuse who were evaluated for liver transplantation. *Liver Transpl*. 2001;7:581–587.
22. Foster PF, Fabrega F, Karademir S, Sankary HN, Mital D, Williams JW. Prediction of abstinence from ethanol in alcoholic recipients following liver transplantation. *Hepatology*. 1997;25:1469–1477.
23. McCallum S, Masterton G. Liver transplantation for alcoholic liver disease: a systematic review of psychosocial selection criteria. *Alcohol Alcohol*. 2006;41:358–363.
24. Robaeys G, Nevens F, Stärkel P, et al. Previous intravenous substance use and outcome of liver transplantation in patients with chronic hepatitis C infection. *Transplant Proc*. 2009;41:589–594.

25. Nickels M, Jain A, Sharma R, et al. Polysubstance abuse in liver transplant patients and its impact on survival outcome. *Exp Clin Transplant*. 2007;5:680–685.
26. Koch M, Banys P. Liver transplantation and opioid dependence. *JAMA*. 2001;285:1056–1058.
27. Jiao M, Greanya ED, Haque M, Yoshida EM, Soos JG. Methadone maintenance therapy in liver transplantation. *Prog Transplant*. 2010;20:209–214.
28. Kreek MJ. Rationale for maintenance pharmacotherapy of opiate dependence. *Res Publ Assoc Res Nerv Ment Dis*. 1992;70: 205–230.
29. Kanchana TP, Kaul V, Manzarbeitia C, et al. Liver transplantation for patients on methadone maintenance. *Liver Transpl*. 2002;8:778–782.
30. Liu LU, Schiano TD, Lau N, et al. Survival and risk of recidivism in methadone-dependent patients undergoing liver transplantation. *Am J Transplant*. 2003;3:1273–1277.
31. Trzepacz PT, Brenner R, Van Thiel DH. A psychiatric study of 247 liver transplantation candidates. *Psychosomatics*. 1989;30: 147–153.
32. Rodrigue JR, Davis GL, Howard RJ, et al. Psychological adjustment of liver transplant candidates. *Clin Transplant*. 1993;7:228–229.
33. Singh N, Gayowski T, Wagener MM, Marino IR. Depression in patients with cirrhosis: impact on outcome. *Dig Dis Sci*. 1997;42: 1421–1427.
34. Norris ER, Smallwood GA, Connor K, et al. Prevalence of depressive symptoms in patients being evaluated for liver transplantation. *Transplant Proc*. 2002;34:3285–3286.
35. Bianchi G, Marchesini G, Nicolino F, et al. Psychological status and depression in patients with liver cirrhosis. *Dig Liver Dis*. 2005;37:593–600.
36. Martins PD, Sankarankutty AK, Silva Ode C, Gorayeb R. Psychological distress in patients listed for liver transplantation. *Acta Cir Bras*. 2006;21(suppl 1):40–43.
37. Telles-Correia D, Barbosa A, Mega I, Direitinho M, Morbey A, Monteiro E. Psychiatric differences between liver transplant candidates with familial amyloid polyneuropathy and those with alcoholic liver disease. *Prog Transplant*. 2008;18:134–139.
38. Telles-Correia D, Barbosa A, Mega I, Monteiro E. Importance of depression and active coping in liver transplant candidates' quality of life. *Prog Transplant*. 2009;19:85–89.
39. Pelgur H, Atak N, Kose K. Anxiety and depression levels of patients undergoing liver transplantation and their need for training. *Transplant Proc*. 2009;41:1743–1748.
40. Gutteling JJ, de Man RA, Busschbach JJV, Darlington A- SE. Health-related quality of life and psychological correlates in patients listed for liver transplantation. *Hepatol Int*. 2007;1:437–443.
41. Dobbels F, Vanhaecke J, Desmyttere A, Dupont L, Nevens F, De Geest S. Prevalence and correlates of self-reported pretransplant nonadherence with medication in heart, liver, and lung transplant candidates. *Transplantation*. 2005;79:1588–1595.
42. López-Navas A, Ríos A, Riquelme A, et al. Obsessive-compulsive psychological symptoms of patients on the liver transplant waiting list. *Transplant Proc*. 2010;42:3153–3155.
43. López-Navas A, Ríos A, Riquelme A, et al. Psychological characteristics of patients on the liver transplantation waiting list with depressive symptoms. *Transplant Proc*. 2011;43:158–160.
44. Rogal SS, Landsittel D, Surman O, Chung RT, Rutherford A. Pretransplant depression, antidepressant use, and outcomes of orthotopic liver transplantation. *Liver Transpl*. 2011;17:251–260.
45. López-Navas A, Ríos A, Riquelme A, et al. Coping styles of patients on the liver transplant waiting list. *Transplant Proc*. 2010;42:3149–3152.
46. Jurado R, Morales I, Taboada D, et al. Coping strategies and quality of life among liver transplantation candidates. *Psicothema*. 2011;23:74–79.
47. Bonaguidi F, Giovanna Trivella M, Michelassi C, Filipponi F, Mosca F, L'Abbate A. Personality change as defensive responses of patients evaluated for liver transplant. *Psychol Rep*. 2001;88:1211–1221.
48. Trzepacz PT, Maue FR, Coffman G, Van Thiel DH. Neuropsychiatric assessment of liver transplantation candidates: delirium and other psychiatric disorders. *Int J Psychiatry Med*. 1986;16:101–111.
49. Gish RG, Lee AH, Keeffe EB, Rome H, Concepcion W, Esquivel CO. Liver transplantation for patients with alcoholism and end-stage liver disease. *Am J Gastroenterol*. 1993;88:1337–1342.
50. DiMartini A, Twillman R. Organ transplantation and paranoid schizophrenia. *Psychosomatics*. 1994;35:159–161.
51. Mahadeva S, Lynch S, Davies MH. Liver transplantation in an undiagnosed schizophrenic. *J R Soc Med*. 1997;90:563.
52. Coffman K, Crone C. Rational guidelines for transplantation in patients with psychotic disorders: current opinion in organ transplantation. *Curr Opin Organ Transplant*. 2002;4:385–388.
53. Guimaro MS, Lacerda SS, Karam CH, Ferraz-Neto BH, Andreoli PBA. Psychosocial profile of patients on the liver transplant list. *Transplant Proc*. 2008;40:782–784.
54. López-Navas A, Rios A, Riquelme A, et al. Importance of introduction of a psychological care unit in a liver transplantation unit. *Transplant Proc*. 2010;42:302–305.
55. Levenson JL, Olbrisch ME. Psychosocial evaluation of organ transplant candidates. A comparative survey of process, criteria, and outcomes in heart, liver, and kidney transplantation. *Psychosomatics*. 1993;34:314–323.
56. Heinrich TW, Marcangelo M. Psychiatric issues in solid organ transplantation. *Harv Rev Psychiatry*. 2009;17:398–406.
57. Lobbestael J, Leurgans M, Arntz A. Inter-rater reliability of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I) and Axis II Disorders (SCID II). *Clin Psychol Psychother*. 2011;18:75–79.
58. Beck AT, Steer RA, Carbin MG. Psychometric properties of the beck depression inventory: twenty-five years of evaluation. *Clin Psychol Rev*. 1988;8:77–100.
59. Steer RA, Beck AT. Beck anxiety inventory. In: *Evaluating Stress: a Book of Resources*. Lanham, MD, US: Scarecrow Education; 1997:23–40.
60. Trzepacz PT, Mittal D, Torres R, Kanary K, Norton J, Jimerson N. Validation of the delirium rating scale-revised-98: comparison with the delirium rating scale and the cognitive test for delirium. *J Neuropsychiatry Clin Neurosci*. 2001;13:229–242.
61. Cottle WC. *The MMPI: A Review*. School of Education; 1953.
62. Addison CC, Campbell-Jenkins BW, Sarpong DF, et al. Psychometric evaluation of a Coping Strategies Inventory Short-Form (CSI-SF) in the Jackson Heart Study cohort. *Int J Environ Res Public Health*. 2007;4:289–295.
63. Mooney S, Hasssanein TI, Hilsabeck RC, et al. Utility of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) in patients with end-stage liver disease awaiting liver transplant. *Arch Clin Neuropsychol*. 2007;22:175–186.
64. Miller PR, Dasher R, Collins R, Griffiths P, Brown F. Inpatient diagnostic assessments: 1. Accuracy of structured vs. unstructured interviews. *Psychiatry Res*. 2001;105:255–264.
65. Goldberg DP. *Manual of the General Health Questionnaire*. Windsor, UK: NFER Publishing; 2006.
66. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary care evaluation of mental disorders. Patient health questionnaire. *JAMA*. 1999;282:1737–1744.

67. von Ammon Cavanaugh S. Depression in the medically ill. Critical issues in diagnostic assessment. *Psychosomatics*. 1995;36:48–59.
68. Endicott J. Measurement of depression in patients with cancer. *Cancer*. 1984;53(10 Suppl):2243–2249.
69. Akechi T, Ietsugu T, Sukigara M, et al. Symptom indicator of severity of depression in cancer patients: a comparison of the DSM-IV criteria with alternative diagnostic criteria. *Gen Hosp Psychiatry*. 2009;31:225–232.
70. Weinrieb RM, Van Horn DHA, McLellan AT, Lucey MR. Interpreting the significance of drinking by alcohol-dependent liver transplant patients: fostering candor is the key to recovery. *Liver Transplant*. 2000;6:769–776.
71. Twillman RK, Manetto C, Wellisch DK, Wolcott DL. The Transplant Evaluation Rating Scale. A revision of the psychosocial levels system for evaluating organ transplant candidates. *Psychosomatics*. 1993;34:144–153.
72. Maldonado JR, Dubois HC, David EE, et al. The Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT): a new tool for the psychosocial evaluation of pre-transplant candidates. *Psychosomatics*. 2012;53:123–132.
73. Miyazaki ET, Dos Santos Jr R, Miyazaki MC, et al. Patients on the waiting list for liver transplantation: caregiver burden and stress. *Liver Transpl*. 2010;16:1164–1168.
74. Weng L-C, Huang H-L, Wang Y-W, Chang C-L, Tsai C-H, Lee W- C. Primary caregiver stress in caring for a living-related liver transplantation recipient during the postoperative stage. *J Adv Nurs*. 2011;67:1749–1757.
75. Sauer P, Schemmer P, Uhl W, Encke J. Living-donor liver transplantation: evaluation of donor and recipient. *Nephrol Dial Transplant*. 2004;19(suppl 4):11–15.
76. Rosenthal L. Design and implementation of an informed consent process before liver transplantation. *Prog Transplant*. 2008;18:273–283.
77. Liou IW, Larson AM. Role of liver transplantation in acute liver failure. *Semin Liver Dis*. 2008;28:201–209.
78. Menegaux F, Keeffe EB, Andrews BT, et al. Neurological complications of liver transplantation in adult versus pediatric patients. *Transplantation*. 1994;58:447–450.
79. Ghaus N, Bohlega S, Rezeig M. Neurological complications in liver transplantation. *J Neurol*. 2001;248:1042–1048.
80. Guarino M, Stracciari A, Pazzaglia P, et al. Neurological complications of liver transplantation. *J Neurol*. 1996;243:137–142.
81. Beresford TP. Neuropsychiatric complications of liver and other solid organ transplantation. *Liver Transpl*. 2001;7(11 suppl. 1):S36–S45.
82. DiMartini A, Crone C, Fireman M, Dew MA. Psychiatric aspects of organ transplantation in critical care. *Crit Care Clin*. 2008;24:949–981.
83. Huang AS, Schwartz EH, Travis TS, Bourgeois JA. Catatonia after liver transplantation. *Psychosomatics*. 2006;47:451–452.
84. Seetharam P, Akerman RR. Postoperative echolalia and catatonia responsive to gamma aminobutyric acid receptor agonists in a liver transplant patient. *Anesth Analg*. 2006;103:785–786.
85. Kalivas KK, Bourgeois JA. Catatonia after liver and kidney transplantation. *Gen Hosp Psychiatry*. 2009;31:196–198.
86. Goralczyk AD, Meier V, Ramadori G, Obed A, Lorf T. Acute paranoid psychosis as sole clinical presentation of hepatic artery thrombosis after living donor liver transplantation. *BMC Surg*. 2010;10:7.
87. Rothenhäusler H-B, Ehrentraut S, Kapfhammer H-P, et al. Psychiatric and psychosocial outcome of orthotopic liver transplantation. *Psychother Psychosom*. 2002;71:285–297.
88. Russell RT, Feurer ID, Wisawatapnimit P, Salomon RM, Pinson CW. The effects of physical quality of life, time, and gender on change in symptoms of anxiety and depression after liver transplantation. *J Gastrointest Surg*. 2008;12:138–144.
89. Fukunishi I, Sugawara Y, Takayama T, Makuuchi M, Kawarasaki H, Surman OS. Psychiatric disorders before and after living-related transplantation. *Psychosomatics*. 2001;42:337–343.
90. Chiu N-M, Chen C-L, Cheng ATA. Psychiatric consultation for post-liver-transplantation patients. *Psychiatry Clin Neurosci*. 2009;63:471–477.
91. Pérez-San-Gregorio MA, Martin-Rodríguez A, Asián-Chavez E, Gallego-Corpa A, Pérez-Bernal J. Psychological adaptation of liver transplant recipients. *Transplant Proc*. 2005;37:1502–1504.
92. Fukunishi I, Sugawara Y, Takayama T, Makuuchi M, Kawarasaki H, Surman OS. Association between pretransplant psychological assessments and posttransplant psychiatric disorders in living-related transplantation. *Psychosomatics*. 2002;43:49–54.
93. Ozkanlar Y, Nishijima Y, da Cunha D, Hamlin RL. Acute effects of tacrolimus (FK506) on left ventricular mechanics. *Pharmacol Res*. 2005;52:307–312.
94. Campana C, Regazzi MB, Buggia I, Molinaro M. Clinically significant drug interactions with cyclosporin. An update. *Clin Pharmacokinet*. 1996;30:141–179.
95. Miguet M, Monnet E, Vanlemmens C, et al. Predictive factors of alcohol relapse after orthotopic liver transplantation for alcoholic liver disease. *Gastroenterol Clin Biol*. 2004;28:845–851.
96. De Gottardi A, Spahr L, Gelez P, et al. A simple score for predicting alcohol relapse after liver transplantation: results from 387 patients over 15 years. *Arch Intern Med*. 2007;167:1183–1188.
97. Karim Z, Intaraprasong P, Scudamore CH, et al. Predictors of relapse to significant alcohol drinking after liver transplantation. *Can J Gastroenterol*. 2010;24:245–250.
98. Burra P, Germani G, Gnoato F, et al. Adherence in liver transplant recipients. *Liver Transpl*. 2011;17:760–770.
99. Shemesh E, Shneider BL, Savitzky JK, et al. Medication adherence in pediatric and adolescent liver transplant recipients. *Pediatrics*. 2004;113:825–832.
100. Drent G, De Geest S, Dobbels F, Kleibeuker JH, Haagsma EB. Symptom experience, nonadherence and quality of life in adult liver transplant recipients. *Neth J Med*. 2009;67:161–168.
101. Bravata DM, Olkin I, Barnato AE, Keeffe EB, Owens DK. Health-related quality of life after liver transplantation: a meta-analysis. *Liver Transpl Surg*. 1999;5:318–331.
102. Tome S, Wells JT, Said A, Lucey MR. Quality of life after liver transplantation. A systematic review. *J Hepatol*. 2008;48:567–577.
103. Ruppert K, Kuo S, DiMartini A, Balan V. In a 12-year study, sustainability of quality of life benefits after liver transplantation varies with pretransplantation diagnosis. *Gastroenterology*. 2010;139:1619–1629.
104. Weinrieb RM, Van Horn DHA, Lynch KG, Lucey MR. A randomized, controlled study of treatment for alcohol dependence in patients awaiting liver transplantation. *Liver Transpl*. 2011;17:539–547.
105. Beavers KL, Sandler RS, Fair JH, Johnson MW, Shrestha R. The living donor experience: donor health assessment and outcomes after living donor liver transplantation. *Liver Transpl*. 2001;7:943–947.
106. Verbesey JE, Simpson MA, Pomposelli JJ, et al. Living donor adult liver transplantation: a longitudinal study of the donor's quality of life. *Am J Transplant*. 2005;5:2770–2777.
107. Diaz GC, Renz JF, Mudge C, et al. Donor health assessment after living-donor liver transplantation. *Ann Surg*. 2002;236:120–126.
108. Schulz K-H, Kroencke S, Beckmann M, et al. Mental and physical quality of life in actual living liver donors versus potential living liver donors: a prospective, controlled, multicenter study. *Liver Transpl*. 2009;15:1676–1687.
109. Renz JF, Mudge CL, Heyman MB, et al. Donor selection limits use of living-related liver transplantation. *Hepatology*. 1995;22:1122–1126.

110. Sterneck MR, Fischer L, Nischwitz U, et al. Selection of the living liver donor. *Transplantation*. 1995;60:667–671.
111. Nickels MW, Cullen JP, Demme RA, et al. A psychosocial evaluation process for living liver donors: the University of Rochester model. *Int J Psychiatry Med*. 2011;41:295–308.
112. DuBay DA, Holtzman S, Adcock L, et al. Adult right-lobe living liver donors: quality of life, attitudes and predictors of donor outcomes. *Am J Transplant*. 2009;9:1169–1178.
113. Erim Y, Beckmann M, Valentin-Gamazo C, et al. Quality of life and psychiatric complications after adult living donor liver transplantation. *Liver Transpl*. 2006;12(12):1782–1790.
114. Trotter JF, Hill-Callahan MM, Gillespie BW, et al. Severe psychiatric problems in right hepatic lobe donors for living donor liver transplantation. *Transplantation*. 2007;83:1506–1508.
115. Gordon EJ, Daud A, Caicedo JC, et al. Informed consent and decision-making about adult-to-adult living donor liver transplantation: a systematic review of empirical research. *Transplantation*. 2011;92:1285–1296.
116. Fujita M, Slingsby BT, Akabayashi A. Three patterns of voluntary consent in the case of adult-to-adult living related liver transplantation in Japan. *Transplant Proc*. 2004;36(5):1425–1428.
117. Papachristou C, Walter M, Marc W, Frommer J, Frommer J, Klapp BF. Decision-making and risk-assessment in living liver donation: how informed is the informed consent of donors? A qualitative study. *Psychosomatics*. 2010;5:312–319.
118. Kemph JP, Bermann EA, Coppolillo HP. Kidney transplant and shifts in family dynamics. *Am J Psychiatry*. 1969;125:1485–1490.
119. Muslin HL. On acquiring a kidney. *Am J Psychiatry*. 1971;127:1185–1188.
120. Hayashi A, Noma S, Uehara M, et al. Relevant factors to psychological status of donors before living-related liver transplantation. *Transplantation*. 2007;84:1255–1261.