

# Ask the Expert

PSYCHOSOMATIC MEDICINE  
TRANSPLANT ASSESSMENT

***I have been asked to work up a patient who requires a liver transplant; how should I proceed?***

*Reply from José R. Maldonado, M.D.*

In the assessment of any patient being considered as a potential transplant recipient, the main issue is whether he or she meets medical and psychosocial listing criteria. The medical criteria have been relatively well established by the United Network for Organ Sharing (UNOS) and, more specifically, have been defined for liver transplant recipients by the Model for End-Stage Liver Disease (MELD) system developed by the Mayo Clinic.

The issue of psychosocial criteria is less standardized, both regarding tools and techniques used. Even though every organization regulating transplantation procedures recommends or requires *psychosocial evaluations* as a prerequisite for transplantation, the published literature regarding specific instruments that reliably measure psychosocial variables predictive of better transplant outcomes is scarce. In fact, it reveals that transplant programs and psychosocial expert consultants use different techniques and psychosocial eligibility criteria to evaluate prospective transplant candidates (1). Despite these discrepancies, a survey of transplant programs showed that certain conditions were endorsed as “absolute contraindication to transplantation” by 70% of responders (2). These included the following:

- Current addictive drug use
- Active schizophrenia
- Current heavy alcohol use
- History of multiple suicide attempts

- Current suicide ideation
- Dementia

Despite the lack of standardization, as psychiatric consultants we can enhance transplant success by assessing patients for predictive risk factors associated with poor adherence/compliance and thereby enhance the selection process. The way I see it, the goals of a psychosocial pretransplant evaluation should include the following:

- Promoting fairness and equal access to care
- Maximizing optimal outcomes and wise use of scarce resources
- Ensuring that the potential for benefits outweighs surgical risks to the patient by identifying potential risk factors (i.e., substance abuse, compliance issues, or serious psychopathological conditions) that may result in increased risk of postoperative noncompliance and morbidity
- Providing information to develop treatment planning for individuals at high risk:
  - Identifying the patient’s level of neuropsychiatric and cognitive functioning
  - Developing a psychiatric treatment plan to address current psychiatric problems and help minimize preventable problems
  - Implementing appropriate treatments that reduce harm and mitigate risk

Several years ago, in an attempt to eliminate bias and standardize the psychosocial evaluation process for solid organ transplant candidates, my team and I studied the available literature on transplantation and the factors that seem to make a contribution regarding graft success. As a result we have developed a comprehensive pretransplant solid organ evaluation battery: the Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT).

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#### CME Disclosure

José R. Maldonado, M.D., Associate Professor of Psychiatry and Medicine; Chief, Medical and Forensic Psychiatry Section; and Medical Director, Psychosomatic Medicine Program, Stanford University School of Medicine, Stanford, CA

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The scale addresses only psychosocial variables that are supported by evidence-based data for treatment compliance, quality of life, and graft survival (3). According to our review of the literature, the psychosocial factors that appear to better predict patient's adherence and graft survival fall in the following eight domains (which include a total of 18 identified risk factors):

- Environmental variables and social support (3 items)
- Desire/willingness for transplant (1 item)
- Compliance/adherence (1 item)
- Understanding of illness and transplant process (2 items)
- Lifestyle factors (1 item)
- Substance abuse and risk of recidivism (5 items)
- Psychological factors (4 items)
- Truthful versus deceptive behavior (1 item)

Based on the above 18 factors, the SIPAT provides an overall risk severity score for psychosocial factors important in predicting posttransplant behavior, compliance, and graft success. But the five most important risk factors should be a focus of your evaluation.

*Social and Environmental Variables.* Data suggest that social and environmental variables, such as poor financial status and living at increased distance from the transplant center, both play a significant role in inhibiting adherence. Living arrangement (e.g., distance to transplant center and appropriateness of facilities) was found to be a significant risk factor for transplant failure (4, 5). There is no doubt that the family and psychosocial support network play an important role with respect to survival and morbidity (6–11). In fact, in some studies the support from a spouse was one of the most important factors in predicting the success of the transplant (12).

*Nonadherence.* With respect to the issue of treatment nonadherence, poor preoperative adherence with medical treatment and/or restrictions (e.g., not keeping clinic appointments, refusal to comply with pursuing investigations of medical issues with no particular grounds, and self-medication or willfully switching medication doses) seems to persist postoperatively and is the major determinant of postoperative nonadherence (13–15).

*Substance abuse.* The issue of substance abuse is a critical one, and as a result we devoted 5 of 18 assessment items to it. Preoperative alcohol and substance abuse has repeatedly been shown to be an important predictor for postoperative compliance difficulties (5, 16–20). Also, a history of substance abuse has been found to be both highly predictive

of posttransplant substance use and of posttransplant treatment noncompliance (17, 18). Issues to determine include extent of use (abuse versus dependence), time and conditions to substance use cessation, and risk of recidivism. Shapiro et al. (5) considered the following patient groups to be most at risk for poor compliance:

- Patients whose substance abuse has not been in long-standing remission
- Patients whose substance abuse continues after the development of end-organ damage and symptoms
- Patients who ceased use only in the face of acute illness

Abstinence for >6 months before transplant is the only condition that has been shown to significantly lower the rate of relapse (23% versus 79%,  $p=0.0003$ ) (21).

Regarding alcohol abuse, risk factors associated with graft failure include the following (4):

- A history of previous alcohol-related hospitalization
- Lack of or ineffective alcohol rehabilitation
- Failure to accept further alcohol rehabilitation before transplantation

The attitude toward liver transplantation for alcoholic liver disease changed in 1988, when Starzl et al. published data demonstrating that the survival of patients receiving a transplant for alcoholic cirrhosis was not different from the survival of other transplant recipients. Since that report, alcoholic liver disease has become the most common indication for liver transplantation (22).

A review (23) of 96 published studies regarding liver transplantation for alcoholic liver disease revealed that future abstinence (posttransplant) was associated with the following:

- Social stability
- Absence of close relatives with alcohol problems
- Older age
- Lack of repeated alcohol treatment failures
- Good compliance with medical care
- Lack of current poly substance misuse
- Lack of coexisting severe mental disorder

*Nicotine use.* Even smoking tobacco has been shown to adversely affect transplant outcome. Nicotine use dramatically potentiates morbidity and mortality after transplantation. When analyzing survival, patients who were smokers preoperatively had a significantly worse prognosis than nonsmokers. In fact, smoking after transplantation (all transplants) in combination with immunosuppressive

treatment is associated with perioperative morbidity (e.g., malignancy and end-stage renal failure) and mortality, usually associated with cardiovascular events (e.g., myocardial infarction and cerebrovascular accident). Decreased survival associated with nicotine use has been confirmed in cardiac transplant (24), lung transplant (25), kidney transplant (26), and liver transplant (27) recipients, with an associated increased length of hospital stay and cost of care, specifically in smokers who received liver transplants (28).

*Psychiatric variables.* Finally, regarding specific psychiatric variables, most studies cite a strong influence of psychiatric illness on posttransplant morbidity and mortality (29, 30). A study of pretransplant candidates across organ systems found axis I diagnoses to be associated with poorer psychosocial adjustment and health status and axis II disorders to be associated with medical compliance problems (31). Similarly, Dew et al. (30) confirmed that a history of pretransplant psychiatric problems, poor social supports, the use of avoidant coping strategies, and low self-esteem were associated with increased axis I psychiatric problems posttransplant (30). Furthermore, data suggest that transplant candidates and recipients exhibiting high levels of psychological distress in formal testing seem to experience greater mortality rates (32).

Psychiatric problems before transplantation are consistently reported to persist after surgery and are highly associated with nonadherence postoperatively (4, 5, 20, 29, 33–38). The following psychological variables have all been associated with nonadherence after transplantation:

- Depressive disorders
- Anxiety disorders
- Anger/hostility
- Denial
- Personality disorders
- Psychosis
- Suicidality

In summary, the assessment of liver transplant patients pretransplant is challenging and includes potential clinical, ethical, and social factors. Thus, as psychiatric consultants, our job should be to find data regarding those risk factors for which there is evidence supporting predictive value: the presence or absence of functional social support; the extent of substance use; sobriety and conditions under which it was achieved; a history of medical nonadherence; and the presence of psychiatric disorders. These appear to be the most significant factors relating to the success of a transplant. Whenever possible we should use sources of collateral information (e.g., family or friends) to verify the facts provided,

particularly in patients with hepatic encephalopathy. In addition, developing a good collaborative relationship with the social workers and nurse coordinators of the transplant team will be rewarding, because they usually know the patient much better than you do and can provide a wealth of useful and corroborating (or conflicting) information that may be helpful in making decisions regarding the patient's truthfulness with the process. The use of objective diagnostic tools, such as the SIPAT (3), assists clinicians not only in eliminating the emotional factor from the assessment but also in presenting the facts. Our job as consultants should not be to make a determination regarding the patient's worthiness as a candidate but to assist the transplant selection committee in making the best clinical decision based on current available data.

## REFERENCES

1. Withers NW, Hilsabeck RC, Maldonado JR: Ethical and psychosocial challenges in liver transplantation. *J Psychosom Res* 2003; 55:116
2. 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
3. Maldonado J, Plante R, David E: The Stanford Integrated Psychosocial Assessment for Transplant (SIPAT): a new tool for the psychosocial evaluation of solid organ pretransplant candidates. in 55th Annual Meeting of the Academy of Psychosomatic Medicine. Miami, Fla, American Psychiatric Publishing, Inc., 2008
4. Karman JF, Sileri P, Kamuda D, Cicalese L, Rastellini C, Wiley TE, Layden TJ, Benedetti E: Risk factors for failure to meet listing requirements in liver transplant candidates with alcoholic cirrhosis. *Transplantation* 2001; 71:1210–1213
5. Shapiro PAW, Williams D, Gelman I, Foray AT, Wukich N: Compliance complications in cardiac patients. *Am J Psychiatry* 1997; 154:1627–1628
6. Christensen AJ, Turner CW, Slaughter JR, Holman JM Jr: Perceived family support as a moderator psychological well-being in end-stage renal disease. *J Behav Med* 1989; 12:249–265
7. Debray Q, Plaisant O: Pulmonary transplantation. Psychological aspects. The medical context and indications. *Ann Med Psychol (Paris)*, 1990; 148:105–107, discussion 108–109
8. Feinstein S, Keich R, Becker-Cohen R, Rinat C, Schwartz SB, Frishberg Y: Is noncompliance among adolescent renal transplant recipients inevitable? *Pediatrics* 2005; 115:969–973
9. Molassiotis A, van den Akker OB, Boughton BJ: Perceived social support, family environment and psychosocial recovery in bone marrow transplant long-term survivors. *Soc Sci Med* 1997; 44:317–325
10. Schlebusch L, Pillay BJ, Louw J: Depression and self-report disclosure after live related donor and cadaver renal transplants. *S Afr Med J* 1989; 75:490–493
11. Teichman BJ, Burkner EJ, Weiner M, Egan TM: Factors associated with adherence to treatment regimens after lung transplantation. *Prog Transplant* 2000; 10:113–121
12. Dew MA, Goycoolea JM, Stukas AA, Switzer GE, Simmons RG, Roth LH, DiMartini A: Temporal profiles of physical health in family members of heart transplant recipients: predictors of health change during caregiving. *Health Psychol* 1998; 17:138–151
13. Bunzel B, Laederach-Hofmann K: Solid organ transplantation: are there predictors for posttransplant noncompliance? A literature overview. *Transplantation* 2000; 70:711–716
14. Dobbels F, Verleden G, Dupont L, Vanhaecke J, De Geest S: To transplant or not? The importance of psychosocial and behavioural factors before lung transplantation. *Chron Respir Dis* 2006; 3:39–47
15. Rodríguez A, Díaz M, Colón A, Santiago-Delpin EA: Psychosocial profile of noncompliant transplant patients. *Transplant Proc* 1991; 23:1807–1809
16. Berlakovich GA: Wasting your organ with your lifestyle and receiving a new one? *Ann Transplant* 2005; 10:38–43
17. Dew MA, DiMartini AF, De Vito Dabbs A, Myaskovsky L, Steel J, Unruh M, Switzer GE, Zomak R, Kormos RL, Greenhouse JB: Rates and risk factors

- for nonadherence to the medical regimen after adult solid organ transplantation. *Transplantation* 2007; 83:858–873
18. Hanrahan JS, Eberly C, Mohanty PK: Substance abuse in heart transplant recipients: a 10-year follow-up study. *Prog Transplant* 2001; 11:285–290
  19. Kotlyar DS, Burke A, Campbell MS, Weinrieb RM: A critical review of candidacy for orthotopic liver transplantation in alcoholic liver disease. *Am J Gastroenterol* 2008; 103:734–743, quiz 744
  20. Rivard AL, Hellmich C, Sampson B, Bianco RW, Crow SJ, Miller LW: Preoperative predictors for postoperative problems in heart transplantation: psychiatric and psychosocial considerations. *Prog Transplant* 2005; 15:276–282
  21. Mehra MR, Kobashigawa J, Starling R, Russell S, Uber PA, Parameshwar J, Mohacci P, Augustine S, Aaronson K, Barr M: Listing criteria for heart transplantation: International Society for Heart and Lung Transplantation guidelines for the care of cardiac transplant candidates—2006. *J Heart Lung Transplant* 2006; 25:1024–1042
  22. Maldonado J: Liver transplantation in alcoholic liver disease: selection and outcome. *J Psychosom Res* 2003; 55:115–116
  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. Nägele H, Kalmár P, Rödiger W, Stubbe HM: Smoking after heart transplantation: an underestimated hazard? *Eur J Cardiothorac Surg* 1997; 12:70–74
  25. Hojo M, Morimoto T, Maluccio M, Asano T, Morimoto K, Lagman M, Shimbo T, Suthanthiran M: Cyclosporine induces cancer progression by a cell-autonomous mechanism. *Nature* 1999; 397:530–534
  26. Cosio FG, Falkenhain ME, Pesavento TE, Yim S, Alamir A, Henry ML, Ferguson RM: Patient survival after renal transplantation: II. The impact of smoking. *Clin Transplant* 1999; 13:336–341
  27. Borg MA, van der Wouden EJ, Sluiter WJ, Slooff MJ, Haagsma EB, van den Berg AP: Vascular events after liver transplantation: a long-term follow-up study. *Transpl Int* 2008; 21:74–80
  28. McConathy K, Turner V, Johnston T, Jeon H, Bouneva I, Koch A, Clifford T, Ranjan D: Analysis of smoking in patients referred for liver transplantation and its adverse impact of short-term outcomes. *J Ky Med Assoc* 2007; 105:261–266
  29. Dew MA, Ksomas RL, Roth LH, Murali S, DiMartini A, Griffith BP: Early post-transplant medical compliance and mental health predict physical morbidity and mortality one to three years after heart transplantation. *J Heart Lung Transplant* 2009; 18:549–562
  30. Dew MA, Roth LH, Schulberg HC, Simmons RG, Kormos RL, Trzepacz PT, Griffith BP: Prevalence and predictors of depression and anxiety-related disorders during the year after heart transplantation. *Gen Hosp Psychiatry* 1996; 18(6 suppl):48S–61S
  31. Chacko RC, Harper RG, Kunik M, Young J: Relationship of psychiatric morbidity and psychosocial factors in organ transplant candidates. *Psychosomatics* 1996; 37:100–107
  32. Brandwin M, Trask PC, Schwartz SM, Clifford M: Personality predictors of mortality in cardiac transplant candidates and recipients. *J Psychosom Res* 2000; 49:141–147
  33. Achille MA, Ouellette A, Fournier S, Vachon M, Hébert MJ: Impact of stress, distress and feelings of indebtedness on adherence to immunosuppressants following kidney transplantation. *Clin Transplant* 2006; 20:301–306
  34. Cohen L, Littlefield C, Kelly P, Maurer J, Abbey S: Predictors of quality of life and adjustment after lung transplantation. *Chest* 1998; 113: 633–644
  35. Grulke N, Larbig W, Kächele H, Bailer H: Pre-transplant depression as risk factor for survival of patients undergoing allogeneic haematopoietic stem cell transplantation. *Psychooncology* 2008; 17:480–487
  36. Kiley DJ, Lam CS, Pollak R: A study of treatment compliance following kidney transplantation. *Transplantation* 1993; 55:51–56
  37. Kuhn WF, Brennan AF, Lacefield PK, Brohm J, Skelton VD, Gray LA: Psychiatric distress during stages of the heart transplant protocol. *J Heart Transplant* 1990; 9:25–29
  38. Smith C, Chakraborty A, Nelson D, Paradis I, Kesinger S, Bak K, Litsey A, Paris W: Interventions in a heart transplant recipient with a histrionic personality disorder. *J Transpl Coord* 1999; 9:109–113

## NOTES