

Received: 2017.07.30
Accepted: 2017.08.24
Published: 2017.11.16

Successful Post-Transplant Psychiatric Interventions During Long-Term Follow-Up of Patients Receiving Liver Transplants for Alcoholic Liver Disease

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 **Hiroyuki Kimura**
ABCDEFG 2 **Yasuharu Onishi**
ABCDF 1 **Shinichi Kishi**
BDF 2 **Nobuhiko Kurata**
BDF 2 **Satoshi Ogiso**
BDF 2 **Hideya Kamei**
BD 3 **Chisato Tsuboi**
BD 3 **Naoko Yamaguchi**
BDF 1 **Azusa Shiga**
BDF 1 **Mai Kondo**
BD 1 **Yushun Yokoyama**
BD 1 **Fumika Takasato**

1 Department of Psychiatry, Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan
2 Department of Transplantation Surgery, Nagoya University Hospital, Nagoya, Aichi, Japan
3 Transplant Coordination Service, Nagoya University Hospital, Nagoya, Aichi, Japan

BDF 1 **Hiroshige Fujishiro**
BDF 1 **Kanako Ishizuka**
BDF 1 **Takashi Okada**
BCDF 2 **Yasuhiro Ogura**
ADF 1 **Norio Ozaki**

Corresponding Author: Hiroyuki Kimura, e-mail: kimurahi@med.nagoya-u.ac.jp

Conflict of interest: None declared

Source of support: This study was fully supported by a Grant-in-Aid for Scientific Research (C, No. 24591875) from the Japanese Ministry of Education, Culture, Sports, Science, and Technology, and by a grant from the Japanese Society for the Promotion of Science

Case series

Patient: Male, 44 • Male, 44 • Female, 36
Final Diagnosis: Alcohol use disorders in sustained remission
Symptoms: Relapse of alcohol use • stress-related anger/irritation • zolpidem abuse
Medication: —
Clinical Procedure: Psychiatric intervention
Specialty: Transplantology

Objective: Unusual setting of medical care

Background: Around 20–30% of patients who undergo liver transplantation (LT) for alcoholic liver disease (ALD) will resume heavy drinking after LT. It is crucial to control post-transplant relapse of alcohol use, because alcoholic recidivism has been shown to have a negative impact on post-transplant compliance and long-term outcomes of LT recipients. However, there is currently no specific, effective psychiatric intervention for preventing additional alcohol consumption in clinical practice.

Case Report: We present 3 patients who underwent LT for ALD at Nagoya University Hospital who were followed up for prolonged periods (7.2, 8.8, and 11.3 years, respectively), and review the psychiatric interventions employed to address critical situations. Additional alcohol consumption was noted in Case 1, but prompt collaborative care led to stable abstinence. In Case 2, marked anger and irritation were exacerbated as a result of work, but the anger was controlled by anger management. Case 3 abused a minor tranquilizer, but limit-setting resulted in adequate medical adherence.

Conclusions: Transplant teams need to provide comprehensive treatment for alcoholic recidivism to improve long-term health after LT for ALD.

MeSH Keywords: Alcohol Abstinence • Liver Transplantation • Patient Care Team • Preventive Psychiatry

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/906446>



2135 1 — 20

Background

Although alcoholic liver disease (ALD) is the second most common indication for liver transplantation (LT) after cirrhosis caused by viral hepatitis [1], 20–30% of patients who undergo LT for ALD will return to heavy drinking after LT [2]. Such post-transplant relapse of alcohol use is crucial, because alcoholic recidivism has been shown to have negative impacts on post-transplant compliance and long-term outcomes of LT recipients [3]. Based on the results of a Japanese survey of LT for ALD patients [4], the criterion of alcohol abstinence for 6 months used [5,6] for living- and deceased-donor LT registration was changed to abstinence for 18 months for deceased-donor LT [7]. In addition to these abstinence criteria, Nagoya University Hospital carried out psychosocial assessments before transplantation to prevent additional alcohol consumption [8], as shown in Table 1. However, despite these strict criteria, additional alcohol consumption was observed a few years after LT [9], suggesting that long-term follow-up is required in LT recipients.

It was recently shown that the post-transplantation psychosocial functioning of patients who underwent LT for ALD improved to the level seen in healthy adults [10]; however, there is currently no effective psychiatric intervention for preventing additional alcohol consumption in clinical practice. In this study, we evaluated the psychiatric interventions carried out to address the risk of additional alcohol consumption during the clinical courses of patients followed up for prolonged periods (7.2–11.3 years) after LT for alcoholic liver failure.

As noted above, alcohol relapse after LT is a serious problem with a major impact on patient outcomes after LT. We believe that the evidence from the presented cases will provide useful information for the management of ALD LT recipients.

Case Reports

The transplant team at Nagoya University Hospital consists of transplant surgeons, gastroenterologists, transplant coordinators, psychiatrists, and psychologists. The team was started in 2004 and holds interdisciplinary conferences at least once a week. All living donors and recipients were followed up regularly. If psychiatric problems were suspected after living donor or transplant procedures, diagnoses of mental illnesses were made based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [11]. Furthermore, supportive psychotherapy and psychopharmacology were provided for patients with psychiatric symptoms by psychiatrists specializing in transplantation [12].

A total of 116 patients with ALD were referred to Nagoya University Hospital for LT between May 2003 and June 2017.

Table 1. Psychosocial evaluation criteria of LT for ALD.

Criteria A
Abstinence period lasting at least 6 months (LDLT)/18months (DDLTL)
An oath of the abstinence from alcoholic drinking for the future
Patients with alcoholic liver disease need to fulfill criteria A
Criteria B
No presence of psychiatric comorbidity except for alcohol-related mental disease
Adherence to medical treatment
Understand and agree to transplant and support by the family
Being employed or ready to work
The High-Risk Alcoholism Relapse scale can be scored 0, 1, or 2
Criteria C
Re-evaluation 1 month later in cases in which it is difficult to evaluate risk of alcohol use relapse in the initial interview

LT – liver transplantation; DDLT – deceased-donor liver transplantation; LDLT – living donor liver transplantation; ALD – alcoholic liver disease.

Seventy-two patients with ALD were evaluated not only medically for LT by members of the Departments of Transplantation Surgery and/or Gastroenterological Medicine, but also psychosocially by members of the Department of Psychiatry. LT was finally carried out in 8 patients. In this study, we report on the cases that survived more than 7 years (7.2, 8.8, and 11.3 years, respectively), but who unfortunately experienced a relapse of alcohol use or an increased risk of additional alcohol consumption, and who required psychiatric intervention. All cases were diagnosed with alcohol use disorders in sustained remission (according to DSM-5) [11] with no other mental disorders.

The cases were managed in accordance with the “Guidelines for patient privacy protection in medical articles, including case reports, and on presentations at society meetings” prepared by the Japanese Society of Psychiatry and Neurology. The study was approved by the Ethics Review Committee of Nagoya University Graduate School of Medicine (approval no. 15), and all the subjects gave their informed consent to participate.

Case 1

The patient was a 44-year-old man at initial consultation, who had married at age 23 years and had 2 children. He had

inherited a business from his father and was essentially self-employed. He began drinking heavily at the age 30 years because of overwork; although his family recognized his drinking problem, he denied his drinking. His divorce at age 37 years, as well as the death of his son at 40 years, induced even heavier drinking. The duration of harmful drinking was 5 years and daily intake of alcohol was 160 grams. When he was 41, the patient was warned by his family doctor that he would die in the near future if he did not stop drinking. He stopped drinking immediately, but his liver condition worsened and he required LT. After psychosocial evaluation, he was registered for deceased-donor LT. He remained on the waiting list for 3 years before undergoing a deceased-donor LT. The duration of alcohol abstinence before transplantation was 5 years.

After LT, he lived with his girlfriend and returned to his previous job. Adherence to the immunosuppressive regimen was good after LT, but liver transaminase increased due to stenosis of bile duct anastomosis. Three years after his LT, because much more sedative was needed at the time of endoscopic examination, the patient's transplant surgeons suspected that he might have returned to heavy drinking. He admitted that he had resumed heavy drinking with his friends, and was therefore referred to a psychiatrist at the subsequent transplantation medical team conference. He eventually opted for abstinence following psychiatric treatment including psychological education and supportive therapy. He has been followed up regularly by transplant surgeons and recipient coordinators, as well as by frequent psychiatric supervision, and has successfully continued to abstain from alcohol for 6 years. We also discussed this case in a previous study [8].

Case 2

The patient was a 44-year-old man at initial consultation. He had married at the age of 21 years and had 2 children. He was active during childhood and drank his first alcohol at the age of 15 years. After graduating from junior high school, he worked for some companies and then left his home town at the age of 21. Simultaneously, he began to consume alcohol habitually, and continued to drink 2–3 L of beer every day. He started a restaurant business at the age of 41, and this new lifestyle caused his alcohol consumption to increase. His daily alcohol intake reached 200 grams, and he was diagnosed with alcoholic hepatopathy. The duration of harmful drinking was 3 years. He stopped drinking alcohol according to his physician's instructions, but was repeatedly admitted to the general hospital and discharged. He was subsequently referred to the Department of Transplantation Surgery at Nagoya University for an LT, and a deceased-donor LT was performed 2 years later. The duration of alcohol abstinence before transplantation was 6 months. Liver function was good after LT, with good adherence to the immunosuppressive regimen. His

postoperative course was favorable. He lived with his family and his wife worked to help the family budget. His physical strength improved from 6 months after LT. He was reluctant to attend an alcohol-specialized medical institution, and only his wife therefore received psychological education. Both he and his wife denied that he carried out self-destructive massive-volume alcohol drinking.

One year after LT, he started a new, non-alcohol-associated job, but stress-related anger/irritation became marked, making his personal relationships unstable. These circumstances were reviewed at transplantation medical team conferences, and anger management measures (psychotherapeutic technique for anger prevention and control) were initiated based on the considered increased risk of additional alcohol consumption. He was specifically trained to understand/control his anger when it reached a peak, and combined sessions for 3 months improved his anger control, stabilizing his personal relationships. Accordingly, he also avoided any relapse of alcohol use. The patient remained in the same job 5 years after his LT, with no additional alcohol consumption.

Case 3

The patient was a 36-year-old woman at her initial consultation. She was divorced, with 2 children. She had worked for some companies after graduating from senior high school. She first drank alcohol at the age of 17 years and consumed it occasionally thereafter. By the age of 27 years, she was married, but her alcohol intake increased because of her husband's excessive alcohol consumption/gambling/debts, reaching 16.0 g/day. The duration of harmful drinking was 7 years and daily intake of alcohol was 65 grams.

She experienced esophageal varix rupture at the age of 36 years and liver cirrhosis was detected. She was referred to the Department of Transplantation Surgery at Nagoya University to undergo LT. She underwent a deceased-donor LT 1 year later. The duration of alcohol abstinence before transplantation was 6 months. Liver function was good after LT, with good adherence to the immunosuppressive regimen. After discharge, she lived with her children and started a new part-time job, but insomnia was noted and she was prescribed zolpidem (10 mg/day).

The patient requested a large supply of zolpidem because of marked irritation from 7 months after LT. Psychological education regarding adequate psychopharmacology was conducted, but she consulted other psychiatrists and transplantation surgeons in addition to her follow-up doctor's appointments and requested zolpidem, sometimes lying that she had lost her medication. We considered her to be at increased risk of additional alcohol consumption, and her circumstances were reviewed at transplantation medical team conferences. The

possibility that she might abuse zolpidem instead of alcohol was indicated to the patient. Limit-setting was performed so that physicians other than the attending psychiatrist would not prescribe antipsychotic agents to control deviating behaviors. The team members agreed that unified countermeasures should be taken for the patient. The patient was initially dissatisfied with the psychiatric intervention, but subsequently recognized her dependence on zolpidem, similar to the situation for alcohol. Her deviating behaviors gradually reduced over 6 months, and she avoided any relapse of alcohol use.

There was no deviating behavior and no additional alcohol consumption 9 years after LT.

Discussion

In this study, we evaluated the long-term clinical courses (mean, 9.1 years) of 3 patients who underwent LT for ALD, in whom psychiatric interventions were introduced to address the increased risks of additional alcohol consumption.

It is important to prevent additional alcohol consumption in patients following LT for ALD. Additional alcohol consumption among patients with alcohol use-related disorders accounted for 79% of patients in a non-therapeutic-intervention group, compared with only 25–43% in a therapeutic intervention group, suggesting that special interventions may reduce the risk of additional alcohol consumption [13]. Previous studies [14] indicated that patients who underwent LT for ALD had worse psychosocial functioning than those who underwent LT for non-ALD. The long-term clinical courses of patients who underwent LT for ALD have recently been reported, including the additional alcohol consumption rate and predictive factors for additional alcohol consumption [15–17]. However, it is difficult to provide special treatment to prevent additional alcohol consumption in post-transplantation patients over a long period. In Japan, transplant candidates can be listed if they demonstrate sufficient periods of abstinence, leading the patients and their families to consider that all the alcohol-related problems have been overcome, and cooperation between transplantation and alcohol-specialized institutions is thus inadequate. These factors may contribute to an increased risk of additional alcohol consumption.

In Case 1, the patient admitted additional alcohol consumption to the attending (transplantation) physician, and therapeutic psychiatric intervention was then promptly introduced following the weekly transplantation medical team conferences. Although psychological education and supportive psychotherapy were provided, the patient denied alcohol-related

problems and resisted consultations in the Department of Psychiatry. He therefore continued to be followed up by the transplant surgeon and coordinator, with supervision by the psychiatrist, to prevent additional alcohol consumption. Recent studies have also demonstrated the efficacy of collaborative care for depression in the presence of diabetes or heart disease [18], and collaborative care by respective specialists also proved to be effective in the present case.

Anger/irritation was enhanced by new working conditions in Case 2, with increased expressions of anger both at home and during consultations. Anger management strategies have previously been shown to be effective for controlling anger in the presence of alcohol use-related disorders [19]. In this current case, anger management was combined with supportive psychotherapy for 3 months in cooperation with the patient's wife, who found managing her husband difficult. The patient's anger was subsequently controlled, allowing him to maintain stable employment over a long period.

In Case 3, the patient requested a higher dose of a minor tranquilizer and lied about the situation by requesting repeated temporary consultations. Limit-setting is recommended to address such behavior in cancer patients [20]. In this case, the craving for a minor tranquilizer reflected the patient's addictive alcohol consumption, and she received psychological education. The limit-setting strategy was used in combination with supportive psychotherapy, and the patient's deviating behaviors gradually reduced.

Psychiatric interventions may cause mental stress for patients, and it is therefore important to review the individual's critical circumstances and strategies at transplantation medical team conferences.

Conclusions

We extracted information on psychiatric interventions aimed at addressing the risk of additional alcohol consumption in 3 patients who were followed up for prolonged periods after liver transplantation for alcoholic liver failure. Comprehensive treatment for alcoholic recidivism by multidisciplinary transplantation teams is required to improve long-term health after LT for ALD.

Acknowledgements

We thank Susan Furness, PhD, from Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

References:

1. Jaurigue MM, Cappell MS: Therapy for alcoholic liver disease. *World J Gastroenterol*, 2014; 20(9): 2143–58
2. Lucey MR: Liver transplantation in patients with alcoholic liver disease. *Liver Transpl*, 2011; 17(7): 751–59
3. Faure S, Herrero A, Jung B et al: Excessive alcohol consumption after liver transplantation impacts on long-term survival, whatever the primary indication. *J Hepatol*, 2012; 57(2): 306–12
4. Egawa H, Nishimura K, Teramukai S et al: Risk factors for alcohol relapse after liver transplantation for alcoholic cirrhosis in Japan. *Liver Transpl*, 2014; 20(3): 298–310
5. Dew MA, DiMartini AF, Steel J et al: Meta-analysis of risk for relapse to substance use after transplantation of the liver or other solid organs. *Liver Transpl*, 2008; 14(2): 159–72
6. Kawaguchi Y, Sugawara Y, Yamashiki N et al: Role of 6-month abstinence rule in living donor liver transplantation for patients with alcoholic liver disease. *Hepatol Res*, 2013; 43(11): 1169–74
7. Egawa H, Ueda Y, Kawagishi N et al: Significance of pretransplant abstinence on harmful alcohol relapse after liver transplantation for alcoholic cirrhosis in Japan. *Hepatol Res*, 2014; 44(14): E428–36
8. Onishi Y, Kimura H, Hori T et al: Risk of alcohol use relapse after liver transplantation for alcoholic liver disease. *World J Gastroenterol*, 2017; 23(5): 869–75
9. DiMartini A, Dew MA, Day N et al: Trajectories of alcohol consumption following liver transplantation. *Am J Transplant*, 2010; 10(10): 2305–12
10. Pegum N, Connor JP, Young RM, Feeney GF: Psychosocial functioning in patients with alcohol-related liver disease post liver transplantation. *Addict Behav*, 2015; 45: 70–73
11. Association. AP: Diagnostic and statistical manual of mental disorders, Fourth Edition, Text Revision (DSM-5). Washington DC, 2013
12. Kimura H, Onishi Y, Sunada S et al: Postoperative psychiatric complications in living liver donors. *Transplant Proc*, 2015; 47(6): 1860–65
13. Connor JP, Haber PS, Hall WD: Alcohol use disorders. *Lancet*, 2016; 387(10022): 988–98
14. Potts SG. *Transplant psychiatry*. *J R Coll Physicians Edinb*, 2009; 39(4): 331–36
15. Rustad JK, Stern TA, Prabhakar M, Musselman D: Risk factors for alcohol relapse following orthotopic liver transplantation: A systematic review. *Psychosomatics*, 2015; 56(1): 21–35
16. 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(11): 1183–88
17. Lucey MR: Liver transplantation for alcoholic liver disease. *Nat Rev Gastroenterol Hepatol*, 2014; 11(5): 300–7
18. Richards DA, Hill JJ, Gask L et al: Clinical effectiveness of collaborative care for depression in UK primary care (CADET): Cluster randomised controlled trial. *BMJ*, 2013; 347: f4913
19. Walitzer KS, Deffenbacher JL, Shyhalla K: Alcohol-adapted anger management treatment: A randomized controlled trial of an innovative therapy for alcohol dependence. *J Subst Abuse Treat*, 2015; 59: 83–93
20. McLafferty L, Childers JW: Borderline personality disorder in palliative care #252. *J Palliat Med*, 2012; 15(4): 485–86