Research Article

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Predicting alcohol relapse in liver transplant

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A new method for predicting alcohol relapse in patients undergoing liver transplantation for alcohol-related liver failure: Barratt scale

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Abstract

Background and Aim: Alcohol-induced liver disease has become one of the major causes of chronic liver disease worldwide with the increasing use of alcohol in society. The most important step in treatment is cessation of alcohol consumption. In patients with advanced liver disease, the most effective treatment is liver transplantation. Careful evaluation of patients with alcoholic liver disease before transplantation can help identify those at high risk of relapsing.

Materials and Methods: Of a total of 42 patients who underwent liver transplantation for alcohol-related liver failure in our hospital between 2011 and 2022, 26 surviving patients were included in the study. Patient data were analyzed retrospectively. Demographic data, MELD score, history of alcohol consumption, alcohol treatment, post-transplant prognosis and survival were analyzed. The Barratt Impulsivity Scale-11 Short Form (BIS-11 SF) was applied to the surviving patients for impulsivity analysis to predict the possibility of relapse.

Results: Of the 26 patients who were included in the study, all were male. The mean age at transplantation was 53 (31–71) years. Mean MELD score was 22.31 (9–36). 12 patients (46.2%) received living donor liver transplantation and 14 patients (53.8%) received cadaveric liver transplantation. 25 patients (96.2%) had no post-transplant dependence, while 1 patient (3.8%) had post-transplant dependence. 5 patients (19.2%) continued to consume alcohol after transplantation.

Conclusion: In our study, we observed that patients with high motor impulsivity tendency according to BSI-11 SF had alcohol relapse. We believe that revising this scale with more detailed questions for alcohol-dependent liver patients and applying it to patients before transplantation will be effective in better selection for transplantation and guiding patients to appropriate therapy and thus preventing relapse after transplantation.

Keywords: Alcoholic liver disease; liver tranplantation; relapse.

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Introduction

Alcoholic liver disease has become one of the major causes of chronic liver disease in our country and worldwide with the increase and widespread use of alcohol in society.[1] Alcoholic liver disease can manifest in several forms such as alcohol-induced fatty liver disease, alcoholic hepatitis and cirrhosis, and acute liver failure depending on the patient's alcohol consumption and metabolism.[2] Cessation of alcohol consumption is a crucial step in the treatment process.[3] In patients with advanced liver disease, liver transplantation has been shown to be beneficial.[4] Liver transplantation has been performed in patients with alcohol-induced liver failure since the early 1980s.[5] Liver transplantation for alcohol-induced liver failure accounts for approximately 15–20% of all liver transplants performed.[6] Although the expectation is that patients will completely abstain from alcohol use after liver transplantation, the resumption of alcohol use after transplantation is one of the most important concerns in patients with alcohol dependence. Studies report a range of results, with approximately 9.85–74% of patients experiencing a relapse.[7,8] Other studies show a narrower range in rates of alcohol relapse after liver transplantation for alcoholic liver disease from 7%[9] to 29%.[10] The majority of studies found rates in the 10–20% range.[11–14]

Although the use of alcohol after transplantation may appear to be an addictive behavior, the intake of alcohol 1–2 times per week is considered to be tolerable by psychiatrists. However, patients with a history of alcohol dependence might face challenges in moderating their consumption. In addition, relapse is likely to occur in patients with psychiatric comorbidities and those with other addictions, such as smoking.[14,15] For these reasons, a thorough evaluation of patients with alcoholic liver disease before liver transplantation to assess their addiction characteristics can identify those at high risk of relapse. Predicting whether they will use alcohol after transplantation and modifying the unfavorable factors will help both to treat the patient for addiction and to prevent relapse and morbidity after transplantation, thereby improving post-transplant survival.[15]

Materials and Methods

In this study, we reviewed 42 patients who underwent liver transplantation for alcohol-related liver failure in our university hospital between 2011 and 2022. Twelve (28%) patients who had died and 4 (9%) who did not wish to participate were excluded. Twenty-six surviving patients were included in the study group. Patient data were collected retrospectively through the electronic patient file system. Demographic

data, MELD score, history of alcohol consumption reported by the patient and included in the psychiatric evaluations, alcohol treatment, post-transplant prognosis, and survival were analyzed.

The Barratt Impulsiveness Scale-11 Short Form (BIS-11 SF) was administered to the surviving patients to analyze of impulsivity and later to investigate the correlation of impulsivity with relapse rate.[16] The BIS-11 SF is a version of the Barratt Scale of impulsivity, which originally consisted of 30 questions. The original questionnaire has been reduced to 15 questions by factor analysis. The SF has been translated into Turkish in a previous study and its validity has been established for Turkish people. It has also been used previously to study the relationship between impulsivity and alcohol dependence in the Turkish population. However, to the best of our knowledge, this is the first time that it has been used in patients who have undergone liver transplantation for alcoholic liver failure.

The impulsivity of the patients is evaluated by obtaining 3 subgroups as "Non-planning," "Attentional impulsivity," and "Motor impulsivity" according to the sum of the scores of 5 specific questions prepared with a Likert scale. The 1st, 5th, 6th, 11th, and 15th questions are related to non-planning, the 2nd, 3rd, 7th, 8th, and 9th questions are related to attentional impulsivity, and the 4th, 10th, 12th, 13th, and 14th questions are related to motor impulsivity. Although the total score is not conclusive, the cutoff value is determined in accordance with the model used.[16] In our study, to predict alcohol relapse after transplantation, we aimed to determine a cutoff value in this group by applying the BIS-11 SF to patients and to create a model specific to alcoholic liver patients by evaluating its use.

The results of the test were evaluated by factor analysis. SPSS version 26 (IBM, Armonk, New York, USA) was used for data analysis. After descriptive statistics, the normal distribution of continuous variables was assessed by the Kolmogorov–Smirnov test for group comparisons. The Student's t-test was used for pairwise comparisons of normally distributed data. The Mann–Whitney U test was used for pairwise comparisons of non-normally distributed data. The Chi-squared test was used to compare categorical variables. ROC analysis was used to obtain sensitivity and 1-specificity values. The Youden j table was created using the Youden index (sensitivity + specificity −1) to determine the cutoff value. The peak of the distribution was determined in the table and the current peak value of this distribution was determined as the cutoff value.

Results

A total of 26 patients were enrolled in the study. All patients were male in our study group. The mean age at transplantation was 53 years (31–71). Two patients (7.7%) had concurrent hepatocellular carcinoma in addition to alcohol-induced liver damage. The mean MELD score was 22.31 (9–36). Fifteen patients (57.8%) underwent liver transplantation from cadaveric donors, whereas 11 patients (42.2%) had transplants from living donors. Six living donors were from the recipients' children (23.1%), 2 were from unrelated donors (7.7%), 1 was from a spouse (3.8%), 1 was from a brother (3.8%), and 1 was from a distant relative (3.8%) (Fig. 1).

Patients were assessed by dedicated liver transplant psychiatrists using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for substance use disorders. Twenty-three patients (88.5%) had no history of alcohol dependence before transplantation, whereas 3 patients (11.5%) had a history of alcohol dependence before transplantation. The average alcohol use duration was 29.57 years (5–50). All patients attended the liver transplant psychiatry outpatient clinic and were evaluated for their alcohol use post-transplant. For the first 6 months, visits were once every month; however, not all patients were compliant with their visits. At each clinic visit, in addition to general examination, they were also asked about their alcohol use, and depending on their clinical and mental status, statements from themselves or family members, or any suspicion of abuse, blood tests were performed accordingly. Patients with a history of psychiatric medication use and diagnosis were called in more frequently. Drinking 4 or more in 1 day or drinking for 4 or more days consecutively, which would sum to higher than 40 g/d alcohol consumption, was considered dependency. Twenty-five patients (96.2%) did not develop post-transplant dependence whereas 1 patient (3.8%) had post-transplant dependence. Twenty patients did not consume alcohol after transplantation whereas 5 patients (19.2%) continued to consume alcohol to varying degrees without exceeding 40 g/d (Table 1).

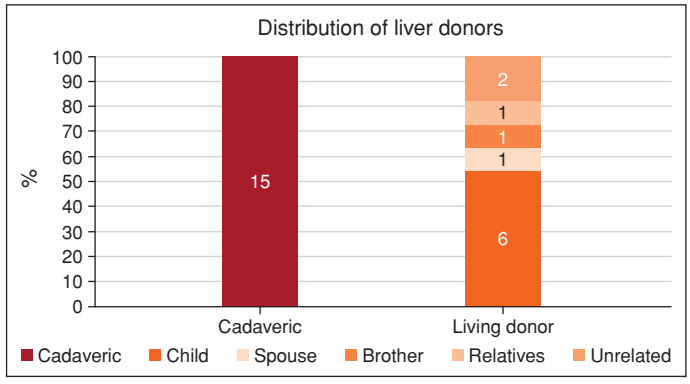

Figure 1. Distribution of liver donors.

Table 1. Demographic and characteristic data

	n=26	%
Gender		
Male	26	100
Female	0	0
Transplant age (mean)	53 (27–71)	
MELD	23.31 (9–36)	
Etiology		
Alcohol	26	100
Concurrent HCC	2	7.7
Graft		
Living donor	11	42.2
Cadaveric	15	57.8
Pre-transplant dependency		
Present	23	11.5
Absent	3	88.5
Alcohol intake post-transplant		
Present	5	19.2
Absent	21	80.8
Alcohol dependence post-transplant		
Present	1	3.8
Absent	25	96.2

MELD: Model for end-stage liver disease; HCC: Hepatocellular carcinoma.

Table 2. BIS-11 SF results

Patient no	Non-planning	Attention	Motor
1	16	8	7
2	14	11	11
3	15	13	10
4	19	14	11
5	18	7	8
6	14	13	13
7	15	10	8
8	12	10	9
9	19	10	7
10	17	11	11
11	16	9	9
12	20	5	6
13	20	9	13
14	20	7	7
15	19	9	11
16	14	11	9
17	15	7	9
18	12	11	11
19	17	11	13
20	18	10	16
21	19	7	9
22	17	8	20
23	18	12	8
24	19	6	7
25	16	11	10
26	16	7	9

BIS-11 SF: Barratt Impulsivity Scale-11 Short Form.

The results of the scales applied to the patients were evaluated in 3 subgroups. Patients were divided into two groups as those who drank alcohol after transplantation (X group) and those who did not (Y group), and their subgroup scores were compared. The subgroup scores of the patients are summarized in Table 2.

According to these data, no significant difference was found between the two groups in the subgroups of non-planning and attention impulsivity. A statistically significant correlation was found between the motor impulsivity subgroup scores of the X and Y groups (p=0.019) (Table 3).

ROC analysis was performed to determine the cutoff value for the motor impulsivity score. In the ROC analysis, the area under the curve was found to be 83.3% and it was found to be a statistically significant parameter (p=0.001). The cutoff value was found to be "12" by Youden analysis. According to the cutoff value, the patients were divided into two groups with low and high motor impulsivity scores. Using the motor impulsivity scoring model, X and Y groups after liver transplantation were compared, and the difference was found to be statistically significant (p=0.010) (Table 4).

Table 3. Comparison of alcohol consumption and subgroups after transplantation

	Post-transplantation alcohol use		
	Present	Absent	p
Non-planning	15.0	17.14	0.069
Attention	10.0	9.38	0.672
Motor	13.0	9.33	0.019

Table 4. Comparison of post-transplant alcohol use and non-use by cutoff score

	Post-transplant alcohol use		
	Present	Absent	p
Motor impulsiveness			0.010
Low (<12)	2 (9.5%)	19 (90.5%)	
High (>12)	3 (60%)	2 (40%)	

Discussion

In our study group of 26, all patients were male. One female patient was transplanted for alcoholic liver disease in our center but exitus was not included in our study. In the literature, a retrospective study from Michigan has investigated the gender disparity of 949 patients with alcoholic liver disease evaluated for transplantation. It was seen that 33% of evaluated patients were female and women were less likely to be listed for transplantation (10% vs. 19%). Furthermore, listed women were found less likely to undergo liver transplantation (42% vs. 47%). It was concluded that because women had more psychiatric comorbidities and were less likely to be listed due to active alcohol and opioid use, early identification, and effective treatment of psychiatric and substance use disorders in women with ALD could improve their transplant eligibility.[17]

In many centers, patients with alcoholic liver failure are mandated to have abstained from alcohol for 6 months after clinical indication for liver transplantation.[18] It is also reported that patients undergoing transplantation should not drink alcohol after transplantation. However, alcohol relapse is seen in patients with irregular and incomplete psychiatric control or highly impulsive dependent patients, resulting in graft loss, and serious morbidity or mortality. For this reason, the 6-month abstinence rule, which has often been shown to be beneficial in the literature, is used as a simple and reliable method[19] and is strictly applied in our university under the control of psychiatric evaluations.

According to the results of the literature review by Lim et al.,[19] alcohol relapse may depend on many factors specific to each center and patient, but the prognosis of relapsed patients is poor in many studies. In order to predict, post-transplant alcohol relapse, several scoring systems have been proposed. Poor social support, psychiatric comorbidities, tobacco use, and noncompliance all have been associated with an increased risk of alcohol relapse. A history of psychiatric disorders, especially depression, lack of a stable relationship, daily alcohol consumption in the years before the evaluation for transplant, dependence on "family or friends" for support after transplant, tobacco use at the time of the evaluation, and lack of understanding of the etiology of alcohol have also

been identified as pre-transplant predictors for relapse.[20] However, interestingly and unlike to some other studies, duration of pre-transplant abstinence and social class by occupation did not predict relapse.

In the study by Gottardi et al.,[14] with a group of 387 patients, the High-Risk Alcoholism Relapse Scale (HRARS), which had previously been applied to small groups of patients, was used to predict alcohol relapse. The HRARS mainly evaluates the duration of heavy drinking, the number of drinks per day, and the number of prior hospitalizations for alcohol abuse. However, the successful results obtained in the studies in which it had previously been used to predict alcohol relapse were not found since the HRARS scale is based on the patient's alcohol consumption.

The Alcohol Relapse Risk Assessment (ARRA) assesses nine factors including the absence of hepatocellular carcinoma, tobacco dependence, continued alcohol use after liver disease diagnosis, low motivation for alcohol treatment, poor stress management skills, lack of rehabilitation, limited social support, and lack of nonmedical behavioral consequences. The high scores have been associated with alcohol relapse, but these results have not been replicated by other studies.[21]

The Stanford Integrated Psychosocial Assessment for Transplant (SIPAT) was used in a prospective study of heart, lung, liver, and kidney transplant recipients. SIPAT scores were significantly correlated with the likelihood of poor medical and psychosocial outcomes, although it was not shown to predict relapse in liver transplant patients.[22]

Another score, the University of Michigan Alcoholism Prognosis Score was developed to stratify potential transplant candidates into low- and high-risk categories for alcohol relapse. It incorporates knowledge of alcoholism, social stability, and factors that suggest a favorable prognosis for staying sober.[23]

In a study of 61 patients, 12 (20%) of whom had a recurrence, Gish et al.[24] found that poor compliance, with a relative risk of 20.9 (95% confidence interval [CI], 5.6–78.3; $p<0.001$), and personality dysfunction, with a relative risk of 6.0 (95% CI, 1.9–18.7; $p=0.002$), independently predicted the likelihood of recurrence. They concluded that specific behaviors and psychiatric diagnoses could be used to select patients at high risk for alcohol use before and after liver transplantation. They concluded that specific behaviors and psychiatric diagnoses could be used for selection of patients at high risk for alcohol use before and after liver transplantation.

It is important to identify patient factors associated with alcohol relapse and interventions to prevent relapse. In our study, 5 patients resumed alcohol consumption after transplantation, but their general health did not deteriorate. However, graft rejection or recurrence of alcoholic liver failure in long-term follow-up is highly probable, according to the literature. We believe that it may be insufficient to consider only the use of alcohol or the social history without taking into account the underlying impulsivity of the patient, which creates the addictive pathologies that require medical or psychiatric intervention. Therefore, a scale that accounts for the impulsivity that leads to addiction may be more effective in predicting alcoholic relapse.

The Barratt scale was developed by Ernest S. Barratt[25] to relate impulsivity to anxiety and psychomotor performance. The 30-item BIS-11 scale, which has been updated with many subscales over time and is now in its 11th version, is a self-report tool used to assess the personality and behavioral structure of impulsivity.[26] However, the use of the scale outside the clinic and in different languages/cultures may lead to inaccurate results.[27]

In recent years, the concept of impulsivity has been increasingly evaluated in behavioral and clinical settings. In order to use the Turkish version of the Barratt Impulsiveness Scale 11, it must first be translated into Turkish by several different and independent translators and then reviewed by a professional translator whose native language is English. These studies have been previously validated and the use of this scale in the Turkish population has been investigated.[28] In their study, Gulec et al.[28] concluded that the test was reliable, yielded consistent responses, and thus had a factor structure similar to the original test. It was concluded that this test can be used in non-clinical settings as well as with psychiatric patients.

In a recent study, Durmuş et al.[29] evaluated the Turkish version of the BIS-11 SF in clinically and non-clinically followed adolescents who were diagnosed with ADHD. The BIS-11 SF was administered to 116 psychiatric outpatients and 175 middle and high school students in combination with the aggression subscale of the Childhood Behavior Checklist (CBCL) and other tests of hyperactivity, impulsivity, and anger problems. At the end of the study, the BIS-11 SF was found to be reliable and valid.

Another study involving 40 male alcohol-addicted patients and 40 male heroin, studied BIS in addicted patients in the Turkish population, showed that there was impaired decision-making and impulsiveness in these patients ($p<0.05$). It was concluded that awareness of the interoceptive processes may be disturbed in addiction disorders, and decision-making could be impaired in addicted individuals.[30]

The Barratt Impulsivity Scale, the Michigan Alcoholism Screening Test, and the Maudsley Obsessive Compulsive Inventory were used in 85 patients in the Turkish population diagnosed with alcohol addiction to assess the relationship between impulsivity, compulsivity, and the severity of alcoholism, respectively. The impulsivity score of the early-onset alcohol-addicted group was higher than that of the late-onset alcohol-addicted group and a positive correlation was found between impulsivity and compulsivity in terms of all sub-groups of BIS-11.[31]

Impulsivity with BIS-11, among other parameters, was also assessed in 60 patients who completed the inpatient program for alcoholism and 28 patients who left their treatment. Addiction to novelty and rewards, personality traits that are thought to lead to addiction were found to be significantly different in patients who completed therapy.[32]

In our study, according to the results obtained with the BIS-11 SF, which we applied to patients undergoing liver transplantation for alcohol-related liver failure, the likelihood of alcohol relapse increases in patients with high motor impulsivity. This shows that even if we are sure that the patient will not relapse to alcohol after transplantation as a result of the pre-transplant evaluation, quantitative data on whether a relapse will develop can be obtained by administering the BIS-11 SF impulsivity test, and a more accurate decision can be made.

Conclusion

In the 60 years since Ernest Barratt explained impulsivity in relation to personality and behaviors, conceptualized impulsivity in psychiatry, and made it scalable, the scale has been used in many different languages and fields to predict people's behaviors and prevent misbehavior. When alcohol is consumed above a certain amount, it turns from a social behavior into addiction. The frequency of liver failure after alcohol addiction is increasing in the world and liver transplantation is the only treatment option at this point. Unfortunately, patients with alcohol addiction cannot be suitable candidates for transplantation unless they quit alcohol. In addition, patients are expected not to consume alcohol after transplantation. Subjective evaluations made before transplantation sometimes yield inaccurate results and alcohol relapse of patients cannot be prevented.

This study showed the possibility of using scales such as the BIS-11 SF test that allows us to evaluate behaviors with quantitative data and thus make more accurate decisions in the follow-up treatment of patients. Our study is a preliminary study and has limitations such as the fact that it was conducted with a scale that has not been used in this patient group before and that it was applied to a small and isolated group of liver transplant patients. Despite its shortcomings, we believe that it is a promising tool and could make a significant contribution to better selection of patients with alcoholic liver disease for transplantation, and in obtaining better results post-transplant with behavioral correction. Further prospective studies with larger groups of patients, perhaps with the inclusion of the impulsivity element in existing scales, will be necessary.

Ethics Committee Approval: The Ege University Clinical Research Ethics Committee granted approval for this study (number: 23-9.1T/9).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – VU; Design – VU, EK, RT; Supervision – SE; Data Collection and/or Processing – EK; Analysis and/or Interpretation – VU, EK, RT; Literature Search – VU, TG, EK, OOS, FG, AU, MZ, SE; Writing – VU, EK; Critical Reviews – VU, TG, OOS, FG, AU, MZ, SE.

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