Liver Transplantation in Alcoholic Patients: Impact of an Alcohol Addiction Unit Within a Liver Transplant Center

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Background: Many concerns about liver transplantation in alcoholic patients are related to the risk of alcohol recidivism. Starting from 2002, an Alcohol Addiction Unit (AAU) was formed within the liver transplant center for the management of alcoholic patients affected by end-stage liver disease and included in the waiting list for transplantation. We evaluated retrospectively the impact of the AAU on alcohol recidivism after transplantation. The relationship between alcohol recidivism and the duration of alcohol abstinence before transplantation was evaluated as well.

Methods: Between 1995 and 2010, 92 cirrhotic alcoholic patients underwent liver transplantation. Clinical evaluation and management of alcohol use in these patients was provided by psychiatrists with expertise in addiction medicine not affiliated to the liver transplant center before 2002 (group A), or by the clinical staff of the AAU within the liver transplant center starting from 2002 (n = 55; group B).

Results: Group B, as compared with group A, showed a significantly lower prevalence of alcohol recidivism (16.4 vs. 35.1%; p = 0.038) and a significantly lower mortality (14.5 vs. 37.8%; p = 0.01). Furthermore, an analysis of group B patients with either ≥6 or <6 months of alcohol abstinence before transplantation showed no difference in the rate of alcohol recidivism (21.1 vs. 15.4%; p = ns).

Conclusions: The presence of an AAU within a liver transplant center reduces the risk of alcohol recidivism after transplantation. A pretransplant abstinence period ≥6 months might be considered, at least in selected patients managed by an AAU.

Key Words: Alcohol Dependence, Alcoholism, Alcohol Addiction Unit, Alcohol Recidivism, Orthotopic Liver Transplantation.

Alcohol Use Disorder represents the first cause of liver cirrhosis in the Western countries (Tilg and Day, 2007). The persistence of alcohol consumption in patients with alcoholic liver disease (ALD) is associated with a significant risk ratio of death (Pessine et al., 2003; Yates et al., 1998). The primary effective strategy for patients with ALD is represented by total alcohol abstinence, because medical and surgical treatments for ALD and its complications have limited success when drinking continues (Yates et al., 1998). When even total alcohol abstinence does not result in a significant improvement of liver function, orthotopic liver transplantation (OLT) represents the gold standard treatment for end-stage ALD (Addolorato et al., 2013; Varma et al., 2010).

However, many concerns about the usefulness of OLT in alcoholic patients are still present, including the unwillingness of the transplant team to transplant patients at risk of recidivism (Kotlyar et al., 2008). Moreover, alcohol use disorder is still often considered a “self-inflicted disease” (Gramenzi et al., 2011), and part of the society considers alcoholic individuals as patients not deserving an OLT (Neuberger, 2007). Thus, the risk of recidivism is often reported as the major justification against OLT eligibility, also considering the issue of organ shortage (Hartl et al., 2011), the long-term survival reduction, and the graft loss in recidivistic patients (Cuadrado et al., 2005). On the other hand, patient survival rates for ALD are significantly higher than those of patients transplanted for other etiologies (Burra et al., 2010), in particular when recidivism does not occur.

There is a highly variable rate of recidivism in alcoholic patients after OLT, with a percentage ranging from 10 to 95% (Björnsson et al., 2005; Lim and Keeffe, 2004),
probably due to several factors, including different approaches to manage these patients and the lack of consensus on the definition and classification of alcohol consumption (e.g., recidivism, lapse, and relapse) after OLT (Gramenzi et al., 2011).

At present, although predictors of post-OLT recidivism have not been clearly identified (Mackie et al., 2001), a requirement of at least 6 months of total alcohol abstinence before OLT is generally adopted (Neuberger, 2007). However, the validity of the “6-month rule” has been questioned and deemed arbitrary (Gramenzi et al., 2011). Moreover, a higher number of alcoholic patients are likely to achieve long-term total alcohol abstinence, if they are followed by a specialized clinical team that can provide a comprehensive evaluation of the patients’ alcohol use or misuse, and plan specific therapeutic approaches, including, for example, multimodal approaches that include both a psychological and a pharmacological component (Addolorato et al., 2005; EASL, 2012; O’Shea et al., 2010). However, most of the transplant centers use an external team of psychiatrists, social workers, and psychologists to evaluate alcohol use in patients undergoing OLT (Kotlyar et al., 2008), and, the presence of a specialized Alcohol Addiction Unit (AAU) within a transplant center is not routine (Björnsson et al., 2005).

In the Departments of Internal Medicine and Surgery at the Gemelli Hospital (Rome, Italy), patients undergoing OLT received an external psychiatric evaluation for their alcohol use before 2002. Starting from 2002, an AAU was formed and its clinical staff works within the Gemelli OLT group to provide the clinical evaluation and management of alcohol use in patients undergoing OLT.

The main goal of the present retrospective study was to evaluate the impact of the presence of an AAU within the liver transplantation center, on the prevalence of alcohol recidivism in alcoholic patients who underwent OLT. Specifically, these variables were evaluated comparing patients who underwent OLT before or after 2002 (i.e., when the AAU was integrated into the liver transplantation center). Finally, difference in the rate of alcohol recidivism considering the length of alcohol abstinence before OLT was evaluated.

PATIENTS AND METHODS

Alcohol Addiction Unit

The AAU was formed in 1998 in the Department of Internal Medicine of Gemelli Hospital, Catholic University of Rome. The AAU is dedicated to the clinical evaluation, management, and treatment of patients affected by alcohol use disorder. Clinicians working in this unit are board-certified internists, physicians in training and psychologists, with expertise in alcoholism, hepatology, and neuroscience. Patients are usually evaluated as outpatients, but hospitalization is available as the clinical situation may dictate. The clinical staff of the AAU joined the liver transplantation center Group of the Gemelli Hospital in 2002 to provide expert clinical support in the evaluation, management, and treatment of patients with alcohol use disorder affected by end-stage ALD. Staff of the AAU provides a multimodal approach to help patients achieving and maintaining alcohol abstinence; monitors abstinence in those patients on the OLT waiting list; and offers therapeutic support to prevent recidivism before and after OLT. Members of the AAU participate in weekly meetings with all the other members of the Gemelli OLT group and play a key role in the final decision of those issues related to patients’ alcohol use, such as, for example, including or removing patients from the OLT waiting list, as well as approving in some specific cases the inclusion in the waiting list of patients with <6 months of total alcohol abstinence. Members of the AAU follow up patients in the OLT waiting list or under consideration for inclusion on a weekly basis during the first month, then every other week during the second and third month, and finally every month.

Patients

Between 1995 and 2010, a total of 297 patients affected by cirrhosis underwent OLT at the Gemelli Hospital liver transplantation center. Indications for OLT are shown in Fig. 1. A total of 92 patients who underwent OLT had a diagnosis of alcoholism; an increase in OLT for alcoholic cirrhosis was observed between 2001 and 2009 (Fig. 1). Sociodemographic characteristics of patients are shown in Table 1. The medical records of these patients were reviewed retrospectively. The diagnosis of alcoholism was made based on either the DSM-III-R or the DSM-IV criteria (Diagnostic and Statistical Manual of Mental Disorders, 3rd or 4th revision). The diagnosis of cirrhosis was made on the basis of histological findings, physical examination, or both, biochemical laboratory tests, and diagnostic imaging. Severity of cirrhosis was classified according to the Child-Pugh and the model of end-stage liver disease (MELD) scores.

Patients (n = 92) were divided into 2 subgroups: patients who were followed up by the AAU (n = 55, 60%); and patients who were

![Fig. 1.](image-url)
was considered equal to 12 g of absolute alcohol). The main consideration was the number of standard drinks consumed (a standard drink was considered equal to 12 g of absolute alcohol). The main biomarkers of alcohol consumption (γ-glutamyltransferase, mean cellular volume, aspartate aminotransferase/alanine aminotransferase > 2) were evaluated in all patients, even considering their poor specificity rate in the pre-OLT period (EASL, 2012). Breath-alcohol concentration (BAC) and, starting from 2007, carbohydrate-deficient transferrin were also evaluated in patients followed at the AAU.

**Alcohol Recidivism After OLT**

As total alcohol abstinence is required after OLT, alcohol recidivism was defined as any alcohol intake after liver transplantation (EASL, 2012). Recidivism includes both alcohol relapse and lapse. Alcohol relapse was defined as a daily alcohol intake of more than 4 drinks or an overall consumption of 14 drinks or more per week during at least 4 weeks (Dumortier et al., 2007). We deemed alcohol lapse as any episode of alcohol consumption not classified as relapse. Alcohol recidivism (lapse and/or relapse) was evaluated at each follow-up visit as described before.

**Outcome**

The primary outcome of the study was the difference in alcohol recidivism, between patients followed at the AAU since 2002 and those not followed because seen before 2002. Difference in mortality rate was also evaluated between the 2 groups of patients.

The secondary outcome was the difference in alcohol recidivism between patients with a pre-OLT alcohol abstinence ≥ 6 months and those with a pre-OLT alcohol abstinence <6 months followed by the AAU. No patients with abstinence <6 months were transplanted among those not followed at the AAU.

**Statistical Analysis**

Several techniques were used to analyze the available data. First, a purely descriptive analysis was carried out to summarize each variable studied, both numerical and categorical, through a number of common procedures such as tabular and/or graphical displays and standard measures of data location (mean, quantiles) and dispersion (standard deviation). Moreover, possible relationships among the variables were preliminarily explored by the use of Pearson correlation coefficient (for couples of numerical variables) and contingency tables (in the case of categorical variables). Then, standard 2-sample t-tests were performed to compare mean values of the various numerical variables for 2 specific groups of patients, for instance those followed by the AAU and those not followed. In the case of categorical variables, comparisons of proportions (e.g., proportions of deceased patients) between the 2 groups selected were made by running 2-sample t-tests for the difference of proportions. To study further some categorical variables of interest, a logistic regression approach (based on the logit function) was adopted to model the probability of success (e.g., the probability of recidivism, or that of survival) in relation to a number of possible predictors, both categorical and numerical. Such approach was primarily used to supplement previous analyses based on 2-sample t-tests for proportions; in all these cases, the logistic regression analysis has supported the conclusions derived previously, as reported in the Results section, also adding some valuable information through, for example, the related odds ratios. Finally, the probability of survival for 2 groups of primary interest, that is those followed by the AAU and those not followed, was studied through the use of a Kaplan–Meier model, supplemented with results from log-rank tests performed at different times. Conclusions from such study are drawn in the Results section, both graphically and analytically.

### Table 1. Sociodemographic and Clinical Characteristics of the 92 Patients Who Underwent Liver Transplantation with a Diagnosis of Alcoholism

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Male, n (%)</th>
<th>Female, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD; range</td>
<td>49.39 ± 7.68; 28–69</td>
<td>18.68 ± 6.93; 8–33</td>
</tr>
<tr>
<td>MELD score, mean ± SD; range</td>
<td>9.73 ± 3.12; 5–14</td>
<td>22.94 ± 10.06; 1–45</td>
</tr>
<tr>
<td>Duration of alcohol abuse, years ± SD; range</td>
<td>190.54 ± 100.99; 50–550</td>
<td>100.99; 50–500</td>
</tr>
<tr>
<td>Daily alcohol consumption (g) per day</td>
<td>5 (5.4)</td>
<td>40 (43.5)</td>
</tr>
<tr>
<td>Family history of alcoholism (%)</td>
<td>68 (73.9)</td>
<td>36 (39.1)</td>
</tr>
<tr>
<td>Education (&gt;13 years) (%)</td>
<td>22 (23.9)</td>
<td>7 (7.6)</td>
</tr>
<tr>
<td>HCV (%)</td>
<td>4 (4.3)</td>
<td>13 (14.1)</td>
</tr>
<tr>
<td>HBV (%)</td>
<td></td>
<td></td>
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<tr>
<td>HCC (%)</td>
<td></td>
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</table>

HCV, hepatitis C virus; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; MELD, model of end-stage liver disease.

Not followed up by the AAU (n = 37, 40%) because OLT was performed before 2002.

**Treatment**

Patients followed up at the AAU received a multimodal treatment, in particular clinical and medical management, including counseling and pharmacological treatment. Counseling sessions were provided by the same trained professional staff in individual sessions of up to 30 minutes and focused on craving evaluation and identification of risk factors for possible relapse (Addolorato et al., 2007). Craving was evaluated by visual analog scale and/or by the Italian version of the obsessive compulsive drinking scale (Janiri et al., 2004). Attendance to support groups (e.g., Alcoholics Anonymous) was strongly recommended but not mandatory. Pharmacological treatment consisted in the administration of the GABAB receptor agonist baclofen (10 mg, t.i.d.), a medication that has shown to be useful in reducing alcohol craving and drinking and safe in cirrhotic patients (Addolorato et al., 2007). Baclofen was prescribed to patients who did not show any contraindication, as previously described (Addolorato et al., 2007). In particular, all (n = 55) patients seen at the AAU received clinical and medical management including counseling. 24 patients attended support groups, and 9 patients received treatment with baclofen.

Alcoholic patients transplanted before 2002 were seen by a team of consultant psychiatrists with expertise in addiction medicine external in the liver transplantation center, which provided psychological support every month. The consultant participated monthly in the Gemelli OLT Group meeting. They expressed a formal opinion on the effective abstinence of patients.

**Evaluation of Alcohol Abstinence Before OLT**

Abstinence from alcohol was assessed in all patients using a clinical interview based on patients’ self-report and interviews with family members (Addolorato et al., 2002; Dumortier et al., 2007). Where reports conflicted, the highest estimate was considered. In case of recidivism, information about the number of standard drinks consumed was collected (a standard drink was considered equal to 12 g of absolute alcohol). The main
All the computations needed to carry out the various analyses were done by using the free software R (R Development Core Team, 2012).

RESULTS

Among 92 alcoholic patients who underwent OLT, 22 (23.9%) patients showed alcohol recidivism after OLT, 22 (23.9%) patients died after OLT, 2 (2.1%) patients were lost to follow-up. Characteristics of alcohol abuse in recidivistic and nonrecidivistic patients are reported in Table 2, and the main causes of death are reported in Table 3.

There were no differences in the mean age, mean MELD score, mean pre-OLT length of alcohol abstinence, and mean alcohol intake before OLT between deceased and survived patients.

Analyzing variables before OLT, there was an inverse correlation between duration of alcohol abuse and survival time after OLT (95% CI: −0.62 to −0.17; p = 0.002). There was an inverse correlation between MELD score and survival time after OLT (95% CI: −0.67 to −0.33; p = 0.000001). No significant correlation between MELD score and alcohol intake (p = 0.128) was found.

There was no significant correlation between the duration of alcohol abuse and MELD score (p = 0.707), alcohol intake (p = 0.543), pre-OLT length of alcohol abstinence (p = 0.808).

Impact of AAU on OLT-Related Outcomes

Of the 55 patients followed at the AAU since 2002, 9 (16.4%) patients had alcohol recidivism, 1 (1.8%) patient was lost to follow-up, and 8 (14.5%) patients died after OLT.

Of the 37 patients who were seen before 2002, thus not followed up at the AAU, 13 (35.1%) patients had alcohol recidivism, 1 (2.7%) patient was lost to follow-up, and 14 (37.8%) patients died after OLT.

Use of t-tests showed no differences between the 2 groups regarding the mean age, mean MELD score, mean time of abstinence before OLT, and mean alcohol intake (Table 4).

Fig. 2. Percentage of patients who showed recidivism after liver transplantation, and statistical comparison. *p = 0.005. AAU, Alcohol Addiction Unit.

A 2-sample t-test for the difference of proportions revealed that, comparing the 2 groups of patients, those followed at the AAU showed a significantly lower prevalence of alcohol recidivism (16.4 vs. 35.1%; p = 0.038) after OLT; this difference remained statistically significant also after excluding the 18 deceased patients (7 among the patients followed by the AAU and 11 among the remaining patients) together with the 2 drop-out patients (1 in the AAU group and 1 in the other group; 19.1 vs. 52%; p = 0.005) (Fig. 2).

Table 2. Characteristics of Alcohol Abuse in Recidivistic (Lapse or Relapse) and Nonrecidivistic Patients. Numerical Comparison Together with the Corresponding p-Value

<table>
<thead>
<tr>
<th></th>
<th>No recidivism</th>
<th>Recidivism</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of alcohol abuse (years), mean (SD)</td>
<td>22.88 (10.14)</td>
<td>23.20 (10.27)</td>
<td>0.92</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>50.16 (7.08)</td>
<td>46.95 (9.10)</td>
<td>0.09</td>
</tr>
<tr>
<td>MELD score, mean (SD)</td>
<td>18.60 (7.17)</td>
<td>19.00 (6.13)</td>
<td>0.84</td>
</tr>
<tr>
<td>Daily alcohol intake (g), mean (SD)</td>
<td>193.98 (106.34)</td>
<td>172.22 (67.23)</td>
<td>0.56</td>
</tr>
<tr>
<td>Pre-OLT length of alcohol abstinence (months), mean (SD)</td>
<td>17.16 (16.64)</td>
<td>13.37 (10.56)</td>
<td>0.39</td>
</tr>
</tbody>
</table>

MELD, model of end-stage liver disease; OLT, orthotopic liver transplantation.

Table 3. Causes of Death in Patients (All Pts = 22), Divided by Follow-Up at the Alcohol Addiction Unit (AAU; No AAU = 14; AAU = 8)

<table>
<thead>
<tr>
<th></th>
<th>All pts.</th>
<th>No AAU</th>
<th>AAU</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac arrest</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>8</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Neoplasm</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Perioperative mortality</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>HCV recidivism</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hepatic artery thrombosis</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

HCV, hepatitis C virus.

Table 4. Characteristics of Alcohol Abuse in Patients Followed and Not Followed at the Alcohol Addiction Unit (AAU). Numerical Comparison Together with the Corresponding p-Value

<table>
<thead>
<tr>
<th></th>
<th>No AAU (n = 37)</th>
<th>AAU (n = 55)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of alcohol abuse (years), mean (SD)</td>
<td>18.00 (12.34)</td>
<td>23.46 (9.80)</td>
<td>0.252</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>47.97 (8.43)</td>
<td>50.34 (7.06)</td>
<td>0.147</td>
</tr>
<tr>
<td>MELD score, mean (SD)</td>
<td>17.63 (6.65)</td>
<td>19.11 (7.06)</td>
<td>0.404</td>
</tr>
<tr>
<td>Daily alcohol intake (g), mean (SD)</td>
<td>235.71 (95.54)</td>
<td>184.22 (101.03)</td>
<td>0.209</td>
</tr>
<tr>
<td>Pre-OLT length of alcohol abstinence (months), mean (SD)</td>
<td>17.25 (12.89)</td>
<td>15.98 (16.77)</td>
<td>0.743</td>
</tr>
</tbody>
</table>

MELD, model of end-stage liver disease; OLT, orthotopic liver transplantation.
A subsequent logistic regression analysis reinforced this conclusion, showing the impact of the AAU on the probability of recidivism; in fact, patients followed at the AAU showed a significantly lower probability to have alcohol recidivism (OR: 0.23; \( p = 0.007 \)) when compared with patients not followed.

Moreover, patients followed at the AAU showed, through a test for the difference of proportions, a significantly lower prevalence of death with respect to those patients who were not followed up at the AAU (14.5 vs. 37.8%; \( p = 0.01 \)). Logistic regression confirmed that patients followed by AAU showed a significantly lower probability to die after OLT with respect to patients not followed (OR: 0.28; \( p = 0.013 \)).

The analysis by the Kaplan–Meier model is summarized in Fig. 3A, where estimated survival probability curves are plotted for each of the 2 groups of patients, those followed at the AAU and those not followed. A visual inspection of this plot suggests that the 2 curves tend to clearly diverge until the time of 2,000 to 2,200 days, equivalent to about 5 to 6 years. Firmer conclusions are drawn by performing formal log-rank tests for different times of interest, as reported by \( p \)-values in Fig. 3A showing the higher estimated survival probability in patients followed at the AAU. Further insights are given from Fig. 3B, which displays the difference of the estimated survival probabilities of the 2 groups of patients, along with the related confidence bands; clearly, this supplemental plot gives results consistent with those provided by the previous analyses.

Finally, patients followed at the AAU were divided into 2 groups on the basis of the pre-OLT length of alcohol abstinence, using 6-month as the cutoff. To study alcohol recidivism properly, the 2 patients with missing abstinence time, together with 7 deceased patients and a single dropout were excluded from the analysis, resulting in a final group of 45 patients. A total of 19 patients (42.2%) showed a pre-OLT length of alcohol abstinence <6 months (4.10 ± 1.66 months), while 26 patients (57.8%) showed a pre-OLT length of alcohol abstinence ≥6 months (23.00 ± 15.96 months). There were no significant differences in term of alcohol recidivism (4/19 [21.1%] vs. 4/26 [15.4%]; \( p = 0.623 \)) after OLT between the 2 groups (Fig. 4). This conclusion was supported by a logistic regression analysis, showing no significant impact of alcohol abstinence time before OLT on alcohol recidivism (\( p = 0.624 \)), after OLT. Moreover, a 2-sample \( t \)-test for proportions showed no significant difference in mortality after OLT between the 2 groups (3/22 [13.6%] vs. 4/31 [12.9%]; \( p = 0.94; \) Fig. 4). In this case, 2 patients with missing abstinence time were excluded from the total group of patients followed in the AAU.

Of the 9 patients treated with baclofen, none showed alcohol recidivism after OLT. There were no differences in terms of mean age, mean MELD score, mean alcohol intake, pre-OLT length of alcohol abstinence between patients who received baclofen and those who did not receive the drug.

Patients with Coinfection(s) and Complications

Of the 92 alcoholic patients, 33 (35.9%) also had a diagnosis of chronic viral infection. In particular, 22 (23.9%)
patients presented with HCV infection, 7 (7.6%) with HBV infection, and 4 (4.3%) with HBV and HCV coinfection.

A total of 13 (14.1%) alcoholic patients were complicated by hepatocellular carcinoma (HCC); of these, 4 (4.3%) had HCV coinfection and 1 (1.1%) had HBV coinfection. All HCC patients met Milan’s criteria for eligibility to OLT.

Two-sample t-tests revealed that patients affected by chronic viral infection, and in particular those affected by HCV, showed a significantly lower duration of alcohol abuse ($p = 0.044$; $p = 0.0397$, respectively), a significantly lower age ($p = 0.044$; $p = 0.029$, respectively), and a significantly higher quantity of mean alcohol intake ($p = 0.059$; $p = 0.035$, respectively) with respect to patients with only an alcoholic etiology of the liver disease. No other significant relationships emerged between viral infections and/or HCC and the other variables considered.

**DISCUSSION**

The present study shows that the presence of an AAU within a liver transplant center reduces alcohol recidivism in alcoholic patients after OLT.

Many issues on the appropriateness of OLT in alcoholic patients are still present. Most of the concerns are related to the risk of alcohol recidivism often reported as the major argument against OLT eligibility (Burra et al., 2000; Gramenzi et al., 2011; Neuberger, 2007). Data from literature show, however, a high variability of recidivism prevalence (Björnsson et al., 2005; Burra et al., 2010; Gramenzi et al., 2011) and this variability could be related to the different management of patients, provided by different professional figures and to different referral settings (i.e., hepatology, surgery, or psychiatry outpatients).

In the present study, the prevalence of alcohol recidivism after OLT in our liver transplantation center was 35.1% (50.0% excluding deceased patients) until 2001; this percentage is consistent with data from other Italian and European liver transplant centers (Burra et al., 2000, 2010). The establishment of an AAU within our liver transplant center determined both an increase in the number of OLTs for alcoholic cirrhosis (Fig. 1) and a significant reduction in the prevalence of alcohol recidivism after OLT. The presence of a specialized staff as in the AAU might have reduced surgeons’ reluctance to transplant alcoholic patients and provided patients with a specific clinical support able to increase their ability to achieve and maintain the total alcohol abstinence.

There are several aspects related to alcohol recidivism after OLT that play a very important role. In fact, alcohol recidivism affects survival of these patients (Faure et al., 2012) due to hepatic damage and pulmonary and pancreatic complications (Lucey et al., 1997; Pageaux et al., 2003). Alcohol recidivism is also associated with a higher incidence of graft loss due to poor compliance to the immunosuppressive therapy (Pageaux et al., 2003) and it is also associated with an increased number of complications that require hospitalization and may even determine the loss of the transplanted organ (Lucey et al., 1997). All of these factors result in a significant increase in social and economic costs. Furthermore, alcohol recidivism could be a reason of public disquiet over distribution of donor livers to those with ALD and could affect organ donation (Neuberger, 2007) worsening the organ shortage and lowering the priority for access to OLT for patients with ALD.

Several approaches have been evaluated to reduce alcohol recidivism in alcoholic patients after OLT, but there is no a standardized approach, and available data are few and often controversial. In some liver transplant centers, alcoholic patients are encouraged to attend support groups, even if data on the efficacy of such treatment in this cluster of patients are at present lacking. In a pilot study, Georgiou and colleagues (2003) reported that psychosocial interventions could be a valid approach to support motivation in these patients. However, this study was conducted on a limited number of patients, and the efficacy of this intervention on alcohol recidivism after OLT was not evaluated. Björnsson and colleagues (2005) evaluated the impact of the management of alcoholic patients by addiction psychiatrists, social workers, and tutors in the period before OLT and reported a 22% prevalence of alcohol recidivism in the treated group versus 48% in the untreated group (Björnsson et al., 2005). Erim and colleagues (2006) evaluated the impact of psychoeducational therapy in this cluster of patients, showing low rates of alcohol recidivism. However, alcohol abstinence was only evaluated using BAC determinations (Erim et al., 2006). In a recent trial, Weinrieb and colleagues (2011) evaluated the impact of motivational therapy versus standard treatment (counseling or support groups) in alcoholic patients waiting for OLT. A modest effect of the motivational treatment was shown (Weinrieb et al., 2011). The presence of an AAU within a liver transplantation center is not usual, but our study suggests that it could represent a useful approach to reducing alcohol recidivism after OLT in alcoholic patients.

In the present study, a significantly lower prevalence of mortality was found in patients followed at the AAU with respect to patients not followed at the AAU. This observation
could be related to several factors not related to the presence of AAU, that is, the improvement of surgical techniques, the increased practice with liver transplantation procedures, intensive care management, and immunosuppressive therapies over time, even considering that some deaths happened perioperatively. However, this result could be at least partially related to the decrease in alcohol recidivism in patients followed at the AAU, a conclusion consistent with previous data showing that alcohol relapse impairs long-term post-OLT survival (Cuadrado et al., 2005; Faure et al., 2012).

An analysis of the subgroup of patients followed at the AAU indicated no significant differences in alcohol recidivism and mortality between patients transplanted with a pre-OLT length of alcohol abstinence <6 or ≥6 months.

At present, the “6-month rule” is generally used to reduce the risk of recidivism risk after OLT (Lucey et al., 1997, 1998); however, this approach has been questioned and deemed arbitrary and not evidence based (Gramenzi et al., 2011). Some studies report that reducing this time could increase the recidivism risk after OLT (Tandon et al., 2009); therefore, patients with an alcohol abstinence time shorter than 6 months (including patients affected by alcoholic hepatitis) should be excluded from transplantation programs. There is growing evidence, however, that the “6-month rule” is unable to predict alcohol recidivism risk (DiMartini et al., 2006; Kelly et al., 2006). Alcohol abstinence time usually produces an improvement of liver function, and a period of total alcohol abstinence is a mandatory criterion for the eligibility to OLT. However, in some patients, the overall clinical status does not allow for a 6 months waiting time, that is, patients with severe alcoholic hepatitis (Brown, 2011; Mathurin et al., 2011) or advanced liver disease. With the limits of the retrospective design, the present study suggests that the pre-OLT abstinence time could be shortened, at least in selected patients followed up in a specialized AAU. In this regard, some reports already support this hypothesis (Lucey, 2002; Neuberger, 2007) and some investigators suggest that the cutoff could be reduced to >3 months in selected patients (Hartl et al., 2011). Future prospective studies are needed, however, to shed light on this point.

A small subgroup of patients received a pharmacological treatment with baclofen as part of the multimodal treatment provided at the AAU. No patients in this subgroup showed alcohol recidivism after OLT. This preliminary observation is consistent with the ability of baclofen to reduce alcohol craving and drinking and promote abstinence in patients with severe liver disease (Addolorato et al., 2007) and tentatively suggest the use of baclofen in alcoholic patients undergoing OLT. Larger prospective studies will be needed to evaluate the potential use of baclofen before and after OLT to prevent alcohol recidivism.

In conclusion, the present study, with the limitations of the retrospective monocentric design and of the small sample size, indicates that the presence of an AAU within a liver transplantation center reduces alcohol recidivism after OLT. Based on this observation, future prospective multicenter studies using a validated and standardized method are needed to further explore this clinical approach that has the potential to significantly reduce the social and economic costs of alcohol recidivism after OLT.

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APPENDIX 1: GEMELLI OLT GROUP

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