

Editorial

Alcoholic Liver Disease and Orthotopic Liver Transplantation

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Alcohol consumption is the third leading cause of preventable death [1,2]. It is responsible for 5.9% of global deaths [1], with 3.3 million deaths per year.

Alcohol Use Disorders (AUDs) are continuously increasing worldwide with the inclusion of countries with strong economic growth like China (3). Currently AUDs represent 5.5% of the global burden of disease and 4.6% of the Disability-Adjusted Life Year (DALY).

The more involved disciplines are cardiology, neurology and hepato-gastroenterology.

Alcohol is one of the most common causes of liver disease after the Hepatitis C Virus (HCV). 80% of deaths from liver disease, 60% of cirrhosis and 50% of deaths from cirrhosis are alcohol related. In addition, the association between alcohol dependence and HCV infection is the primary cause of hepatocellular carcinoma (HCC) [4, 5]. With the introduction of new Direct-Acting Antivirals (DDAs) during the next few years alcohol will become the primary cause of liver disease and Liver Transplantation (LT) [6]. Alcoholic Liver Disease (ALD) is the most common alcohol-related medical complication.

Important factors are the amount, the duration and the type of consumption (binge drinking or daily consumption). In addition, associated risk factors (e.g. HCV and metabolic syndrome) encourage and accelerate ALD.

The risk of harm increases significantly for variable dosages of between 10 and 20 grams of ethanol per day [2].

60-100% of patients will develop steatosis and 20-40% will develop NASH. Genetic factors and factors related to lifestyle greatly affect this step. The liver-intestine interaction is decisive; the alteration of intestinal permeability and bacterial overgrowth determine the translocation of lipopolysaccharides (LPS). The next step is the production of TNF- α and other proinflammatory cytokines. The binding between TNF / TNFR1 results in inflammation, necrosis, necroptosis and apoptosis, as well as the release of Danger-Associated Molecular Patterns (DAMPs). DAMPs ac-

tivate stellate cells and Kupffer cells, and recruit immune cells. 20-40% of cases evolve into cirrhosis, and the onset of HCC varies from 1 to 5% yearly [7,8].

The management of alcohol-related decompensated liver cirrhosis and of Acute Alcoholic Hepatitis (AAH) is very complicated. Transplant management is even more complicated.

Relevant ethical issues emerge (9), especially in relation to the pre-Liver Transplant (LT) abstinence period. In most transplantation centers admission onto the LT list takes place after six months of abstinence. This period is necessary to 'deserve' a LT. This implies, however, a large number of deaths in two particular cases: progressive End-Stage Liver Disease (ESLD) (mortality in about three months in about 76 of cases – Model End Stage Liver Disease over 19), and severe AAH non-responder to medical therapy (mortality in one month approximately 35-40%). Moreover, the need for transplants for AAH represents a very small percentage of cases, usually followed up in a transplant center.

Although the group of patients in need of LT is affected by severe AUD, the percentage of post-LT relapses is significantly lower than in the general population of AUD patients [10].

Dumortier et al. [11] have shown relapse in 18% of cases after one year of follow-up, and De Gottardi et al. [12] in 11.9% of cases after a follow-up of 15 years. In addition, the recurrence of ALD for relapse has been detected in less than 17% of cases, and the percentage of deaths for relapse is less than 5% [7]. These favorable data should be put in relation to the heavy psychological impact on patients facing the difficult path of LT, and to the insertion of an organ in a host with a different genetic background and, therefore, who is more resistant to the development of AUDs and more amenable to strict medical surveillance [10].

It has recently been demonstrated how the pre-LT period of abstinence is not the only parameter to be taken into consideration. To date, in fact, a safe period has not yet been identified. Among the many parameters that must be evaluated, in our opinion the most important are: strong family support, attendance at Self-Help Groups (SHGs) and the presence of a hepato-alcoholologist in the

multidisciplinary transplant team.

The final condition is fundamental: the management of patients with ALD, in fact, is difficult in the presence of two diseases: AUD and liver disease. It is appropriate to act in parallel on two fronts. Achieving abstinence is decisive. During the daily routine an addiction specialist could underestimate the liver problem, while a hepatology specialist often solves the alcohol problem with the simple indication of alcohol abstinence.

It has been shown that the presence of a hepatologist with alcoholological skills guarantees excellent results independently of the period of pre-LT abstinence [13].

However, beyond the necessary technical skills of the multidisciplinary team, the transplanted subject must be wrapped in a protective network where health professionals and families closely cooperate with the indispensable actions of SHGs.

All these conditions allow the attainment not only of a low percentage of post-LT alcoholic relapses, but also better adherence to follow-ups and better management of patients with a psychiatric co-morbidity [14].

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