Prevalence and Predictors of Metabolic Syndrome After Liver Transplantation

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ABSTRACT

Background. The development of metabolic syndrome (MS) after liver transplantation (LT) is a major source of mortality derived from cardiovascular events. The aim of the present study was to determine the prevalence and risk factors of MS after LT.

Methods. One-hundred seventy-four consecutive LT patients from January 2004 to June 2010 surviving longer than 1 year after LT were included. Median follow-up after LT was 48 months. Independent predictors of MS were obtained by means of multivariate logistic regression.

Results. At 3 years after LT, 25.5% of patients reached a body mass index (BMI) ≥30 kg/m^2, 35.6% of patients developed arterial hypertension, 54.2% showed impaired fasting glucose, 22.5% had serum cholesterol >200 mg/dL, and 22.5% showed hypertriglyceridemia >150 mg/dL. The prevalence of MS ranged from 49% to 86% depending on the considered period. The pre-LT variables associated with MS were age at LT (odds ratio [OR], 1.08; $P = .002$), BMI of recipient before LT (OR, 1.23; $P = .001$), serum glucose (OR, 1.02; $P = .005$), and non–heart-beating donor (OR, 1.02; $P = .046$). The post-LT predictors of MS were body weight (OR, 1.04; $P = .005$), arterial hypertension (OR, 1.02; $P = .047$), and serum glucose (OR, 1.02; $P = .011$) at 6 months.

Conclusions. LT patients develop MS in a high proportion and progressively despite current efforts (ie, lifestyle modifications and aggressive management of hypertension, diabetes, and hyperlipidemia). The associated risk factors include age, increased BMI, and pre- and post-LT glucose.

METABOLIC syndrome (MS) is characterized by the presence of abdominal obesity (high waist circumference of 80–90 cm, male or female) and ≥2 criteria as follow: fasting glucose >100 mg/dL, systolic blood pressure (SBP) ≥130 mm Hg and/or diastolic blood pressure (DBP) ≥85 mm Hg, high-density lipoprotein (HDL) cholesterol <40 mg/dL or <50 mg/dL by sex, and triglycerides >150 mg/dL [1,2].

Patients with chronic liver disease have increased rates of obesity (24%–47%) and diabetes mellitus (DM; 20%–47%) than the general population [3]. On the other hand, nonalcoholic fatty liver disease (NAFLD), which is considered to be a manifestation of metabolic syndrome, is the only rising indication for liver transplantation (LT) nowadays, and therefore a worsening of the metabolic profile is expected among the LT population [4].

Several retrospective studies have shown a prevalence of MS ranging from 44% to 58%. However, the actual impact of MS on overall mortality after LT remains to be established. In a systematic review of 12 observational studies including 4,792 transplant patients, the risk of suffering cardiovascular diseases was 64%, and it was increased 4-fold by the presence of MS [5]. Some risk factors for post-LT MS

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Table 1. Etiology of Cirrhosis of Transplanted Patients and Transplant Indications

Characteristic	*n*	%
Cirrhosis etiology		
Alcohol	85	48.9
Viral	86	49.5
HCV	64	36.8
HBV	20	11.5
Others	2	1.2
Metabolic	4	2.3
Autoimmune	1	0.6
Cholestatic	8	4.6
Toxic	3	1.7
Cryptogenic	9	5.2
Transplant indication		
Liver failure	95	54.6
Hepatocellular carcinoma	56	32.1
HCV	29	17.6 (51.78*)
Non-HCV	27	14.5 (48.22*)
Special indication	23	13.2
Refractory ascites	11	45.8†
Hepatic encephalopathy	6	25†
Recurrent cholangitis	2	8.3†
Neuroendocrine tumor	1	4.2†
Others	4	16.7†

Abbreviations: HCV, hepatitis C virus; HBV, hepatitis B virus.
*Percentage in patients transplanted for hepatocellular carcinoma.
†Percentage in patients transplanted for special indications.

have been identified, including pre-LT DM, high pre-LT BMI, poor graft function, age, post-LT renal dysfunction, and certain aspects of immunosuppression, particularly the use of calcineurin inhibitors and corticosteroids, in a dose-dependent manner. However, most of the evidence comes from retrospective small series, and it is not hard to find conflicting results [6].

The aims of the present study were to determine the prevalence of MS among LT patients and to describe the risk factors involved with the onset of MS after LT.

METHODS

This was a retrospective study including 174 consecutive patients who underwent LT from January 2004 to June 2010 at a single institution and survived >1 year. HIV-positive patients were excluded. Because values of waist circumference were not available, BMI ≥30 kg/m^2 (obesity grade I) was adopted instead, as suggested by the World Health Organization classification. This substitution has been addressed and accepted in the study of the database of the National Institute of Diabetes and Digestive and Kidney Diseases [7].

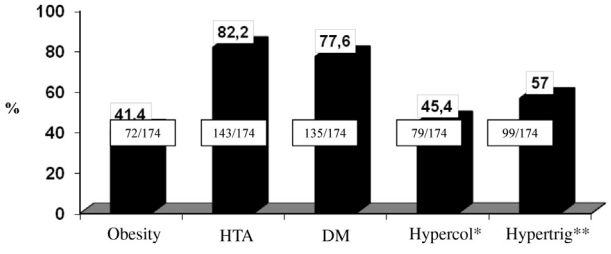

Fig 1. Diseases related to MS in post-LT. *Hypercol: Hypercholesterolemia. **Hypertrig: Hypertriglyceridemia.

For the calculation of cardiovascular risk, scale scores of cardiovascular risk of patients by age and sex based on the predictive panel of the risk of coronary heart disease at 10 years was considered [8]. The evolutionary study was performed every 6 months (1st year) and annually thereafter until a maximum period of 7 years' follow-up.

Statistical Analysis

The quantitative variables were expressed as mean ± SD. Continuous variables were compared with the use of parametric Student *t* test and nonparametric continuous variables with the use of Mann-Whitney *U* test. The normal distribution was assessed with the use of the Kolmogorov-Smirnov test. For categoric variables, chi-square test or Fischer exact test were used. Changes in categoric or continuous in the post-LT variables were studied by means of the analysis of variance for paired measures or the McNemar test.

To identify independent predictors of post-LT MS, multivariate logistic regression analysis was used. A P value of <.05 was the criterion to include, and $P > .10$ was the criterion to eliminate variables from the model. In that analysis, all possible interactions were tested and potentially confounding factors controlled. Statistical analysis was performed with the use of SPSS Statistics for Windows, version 17.0 (IBM, USA).

RESULTS

Descriptive Study

Pre-transplantation Variables. The average age of the recipients was 52.14 ± 10.1 years; 133 men (75.6%) and 41 women (24.4%) were included. Average BMI was 27.2 ± 5.6 kg/m^2. Stratifying by baseline body weight, patients were classified as follows: 49 patients with normal weight (28.16%), 77 patients overweight (47.2%), 28 patients with grade I obesity (17.2%), 6 patients with grade II obesity (3.7%), and 3 grade III (morbid) obesity patients (1.8%). Among these 174 LT patients, 154 had cirrhosis (88.5%). The major etiologies of liver disease were chronic viral hepatitis and alcohol consumption (49.5% and 48.9%, respectively). A total of 36.7% of patients had active hepatitis C infection. Further baseline characteristics are presented in Table 1.

The analytic parameters were: serum glucose, 122 ± 63.9 mg/dL; serum cholesterol, 137.59 ± 77.09 mg/dL; and triglycerides, 97.07 ± 63.5 mg/dL. Twenty-eight of the transplantations took place in 2004, 28 in 2005, 24 in 2006, 21 in 2007, 25 in 2008, 31 in 2009, and 17 in 2010. The average Model of End-Stage Liver Disease (MELD) score was 14.09 ± 5.03.

Donor Features. The average age of donors was 47.2 ± 17.2 years. Fifty-five were women (31.3%). Donor BMI was 26.2 ± 3.7 kg/m^2. The classification of the donors according to weight was as follows: normal weight in 72 donors (41.37%), overweight in 83 donors (47.2%), grade I obesity in 15 donors (8.5%), grade II obesity in 2 donors (1.1%), and morbid (grade III) obesity in 2 donors