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Excess body weight, liver steatosis, and early fibrosis progression due to hepatitis C recurrence after liver transplantation

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Abstract

AIM: To investigate how weight gain after OLT affects the speed of fibrosis progression (SFP) during recurrent hepatitis C virus (HCV) infection of the graft.

METHODS: Ninety consecutive patients (63 males, median age 53 years; 55 with HCV-related liver disease), transplanted at a single institution, were studied. All were followed for at least 2 years after OLT and had at least one follow-up graft biopsy, performed not earlier than 1 year after the transplant operation. For each biopsy, a single, experienced pathologist gave an estimate of both the staging according to Ishak and the degree of hepatic steatosis. The SFP was quantified in fibrosis units/month (FU/mo). The lipid metabolism status of patients was summarized by the plasma triglycerides/cholesterol (T/C) ratio. Body mass index (BMI) was measured before OLT, and 1 and 2 years after it.

RESULTS: In the HCV positive group, the highest SFP was observed in the first post-OLT year. At that time point, a SFP ¡Ü0.100 FU/mo was observed more frequently among recipients who had received their graft from a young donor and had a pre-transplant BMI value >26.0 kg/m^2. At completion of the first post-transplant year, a BMI value >26.5 kg/m^2 was associated with a T/C ratio ¡Ü1. The proportion of patients with SFP >0.100 FU/mo descended in the following order: female recipients with a high T/C ratio, male recipients with high T/C ratio, and recipients of either gender with low T/C ratio. Hepatic steatosis was observed more frequently in recipients who, in the first post-transplant year, had increased their BMI ¡Ý1.5 kg/m^2 in comparison to the pre-transplant value. Hepatic steatosis was inversely associated with the staging score.

CONCLUSION: Among HCV positive recipients, excess weight gain post-OLT does not represent a factor favoring early liver fibrosis development and might even be protective against it.

Key words: Liver transplantation; Hepatitis C infection; Liver fibrosis; Liver steatosis; Body mass index

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INTRODUCTION

Re-infection by hepatitis C virus (HCV) after liver transplantation (OLT) for HCV-related liver disease is almost universal, but the degree of necro-inflammatory damage and fibrosis deposition in the liver graft varies[1]. In the majority of cases, recurrent hepatitis C is mild. In up to one-third of OLT recipients with recurrent hepatitis C, however, a more severe course is observed, with progression to frank cirrhosis in less than 5 years[2]. The mechanisms associated with early fibrosis progression in this setting are actively investigated but remain poorly understood.

After liver transplantation, most patients gain weight[3], partly because of better health and freedom from pre-transplant dietary restrictions. As a result, within 2 years after the transplant operation, 60% of liver transplantation recipients are either overweight or obese. The role of excess weight post-transplant as a cardiovascular and metabolic risk factor has been widely addressed[4]: whether it may also contribute to graft damage, however, is unclear. Specifically, it is unknown if, in recipients with recurrent hepatitis C, fibrosis occurs earlier and is more severe when the patient is overweight or obese. This is conceivable, though, since data in immune-competent patients with chronic hepatitis C demonstrate that excess body weight leads to steatosis[5-7], acts as a cofactor for fibrosis progression[5,8,9] and represents an independent risk factor for non-response to antiviral treatment[10]. Independently of HCV infection, obesity may cause non-alcoholic steatohepatitis, a disease potentially capable of evolving toward cirrhosis and end-stage liver disease[11-13].

The present retrospective, longitudinal study aimed to investigate the possibility of a relationship between pre- and post-transplant body mass and fibrosis progression during recurrent hepatitis C. The study population included both

HCV positive and negative OLT recipients, in whom the value of body mass index (BMI) evaluated pre transplant and in the first 2 years post-transplant was related to the staging score measured in follow-up liver biopsies, taking into account other factors (pertaining to donor and host) which might have influenced the progression of recurrent hepatitis C.

MATERIALS AND METHODS

Patients

A total of 194 patients received a liver graft from a cadaveric donor between March 1996 and December 2002, at our institution. Insufficient data were available for 53 patients, who died either in the early post-transplant period or were lost to follow-up. Of the remaining 141 patients, 90 consecutive OLT recipients had a minimum follow-up of 2 years after OLT and had been subjected to at least one liver biopsy obtained not earlier than 1 year after OLT, and were included in the present study. Table 1 shows the demographic and clinical characteristics of the studied population. All were maintained in an immunosuppressive regimen that was either cyclosporine- or tacrolimus-based, associated, in the first few months, to corticosteroids. Cyclosporine dosage was calculated to obtain serum levels (measured 2 h after the drug administration) ranging from 800 to 1 200 μg/L in the first 6 wk after transplant and from 600 to 800 μg/L thereafter. Tacrolimus dosage was calculated to obtain pre-dose serum levels ranging from 10 to 15 μg/L in the first 6 wk after transplant and from 5 to 10 μg/L thereafter. Corticosteroid tapering was completed in 8 mo after the transplant in all except six patients (four HCV positive and two HCV negative). Thirty-two out of fifty-five HCV positive patients received antiviral treatment with interferon plus ribavirin due to recurrence of HCV hepatitis, defined as detectable serum HCV-RNA, serum alanine-aminotransferase (ALT) levels above the upper normal limit, Ishak grading score ¡Ý2 and no evidence of rejection. Therapy was intended to be maintained for 12 mo. Antiviral treatment was started at a median time of 11.4 mo (range 0.7-75.9) after OLT and was completed in 17 patients. In the remaining 15 patients antiviral therapy had to be stopped prematurely due to adverse effects. Body weight was measured to the nearest 0.1 kg and height to the nearest 1 cm, with study participants wearing only underwear and no shoes. BMI was calculated as weight in kilograms divided by the square of the height in meters; it was measured pre transplant and one and 2 years after transplantation. In patients with ascites, pre-OLT BMI was calculated subtracting from the body weight the amount of ascitic fluid calculated on the basis of an ultrasound evaluation.

Liver histology In follow-up liver biopsies, grading and staging were scored according to the method of Ishak[14]. Fibrosis progression was evaluated annually in the first 4 years after OLT. It was based on the staging score at the corresponding "per protocol" liver biopsy, or, when unavailable, on the closest "on demand" liver biopsy. The speed of fibrosis progression (SFP), expressed in fibrosis units per month (FU/mo), was calculated for each 1-year time interval after OLT. It was obtained dividing the change observed in the fibrosis score at the end of the pertinent interval of time, with respect to either the transplant operation (for the first post-transplant year) or the previous liver biopsy (for the following years), by the number of months elapsed. The sum of micro- and macro-vesicular liver steatosis was calculated in each liver biopsy and graded as absent, ¡Ü10% or >10%. All histological studies were performed by a single experienced histopathologist (CA).

Table 1 Clinical and demographic characteristics of the studied population

Recipient male gender, *n* (%)	63 (70.0)
Donor male gender, *n* (%)	53 (58.9)
Recipient age at transplantation (yr), median (range)	53 (23-66)
Donor age (yr), median (range)	41 (17-77)
Etiology of liver disease, *n* (%)	
HCV infection	55 (61.1)
HBV infection	12 (13.3)
Alcohol abuse	13 (14.5)
Other, unknown	10 (11.1)
Child–Pugh score pre-transplantation, median (range)	8 (5-14)
Immunosuppressive regimen, *n* (%)	
Tacrolimus-based	69 (76.7)
Cyclosporine-based	21 (23.3)
Antiviral therapy in HCV positive, *n* (%)	32 (58.2)

Categorical variables are expressed as frequencies (%); continuous variables as median (range). HCV: hepatitis C virus.

Statistical analysis

Statistical analysis of data was performed by means of the biomedical statistical software package BMDP Dynamic, Rel. 7.0 (Statistical Solutions, Cork, Ireland). Comparisons of continuous variables from two groups were explored by means of the Mann-Whitney's test. Correlations between continuous variables were performed either using the Spearman rank correlation coefficient or the Pearson product moment after logarithmic transformation of the values. Analysis of variance for repeated measures was employed to ascertain the significance of BMI increase post-OLT with respect to pre-OLT values. Wilcoxon matched pairs signed rank sum test was employed to evaluate modifications of fibrosis progression 2 and 3 years post-OLT in comparison to 1 year post-OLT. The associations between categorical variables were explored by means of the Pearson χ^2 test (in selected cases, with comparison of cross product ratios); if appropriate, the χ^2 test for linear trend was applied. Time-to-event analysis was performed to test whether the function to reach a staging score >2, in HCV positive patients, differed according to gender and BMI recorded pre- and 1 year post-OLT. Stepwise logistic regression analysis with a forward approach was used to evaluate the variables independently associated with a high one year post-OLT SFP. A level of 0.05 (two tailed) was chosen to indicate statistical significance.

RESULTS

BMI pre and post-OLT

BMI values, recorded before OLT, as well as 1 and 2 years post-OLT, are expressed in kg/m^2 and presented as medians (25-75th percentiles). For the entire study population, values were 25.0 (23.0-27.1), 25.4 (23.5-27.5) and 26.0 (23.7-28.4),

respectively (ANOVA for repeated measures, $P<0.05$). Among HCV positive recipients, the corresponding values were 24.7 (23.0-26.6), 25.1 (23.3-27.1) and 25.4 (23.4-28.1), respectively. Among HCV negative recipients, the corresponding values were 25.9 (23.0-28.4), 26.0 (24.0-28.0) and 26.6 (24.2-28.9), respectively. A BMI value ¡Ý35 kg/m^2 (the limit indicating grade two obesity) was recognized before transplant operation in one HCV positive male recipient, who had a value of 38.4 kg/m^2. While 1 year after OLT, none of the recipients reached a BMI value ¡Ý35 kg/m^2, 2 years after transplant, one HCV positive recipient had a BMI value of 36.5 kg/m^2 and one HCV negative patient a BMI value of 37.8 kg/m^2. The BMI values recorded pre-OLT and 1 and 2 years post-OLT were not statistically different between HCV positive and negative recipients. Among recipients belonging to both groups, no association was found between the pre-OLT BMI values and the severity of liver disease, calculated as the Child-Pugh score. Similarly, 1 and 2 years post-OLT BMI values did not differ considering the kind of immunosuppressive regimen in use (cyclosporine- or tacrolimus-based) or the rate of corticosteroid tapering (withdrawal completed before or after 90 d from OLT).

Liver histology

The histological follow-up lasted a median of 48 mo (range, 12-102 mo) in the HCV positive group and 30 mo (range, 12-78 mo) in the HCV negative group. A total of 465 follow-up liver biopsies were performed. In the group of HCV positive patients, the liver biopsies performed in a total of 315 patients, with a median number of five biopsies (range, 1-13) for each patient; protocol biopsies were 106/315 (median: two for each patient). In the group of HCV negative recipients, the liver biopsies performed were in a total of 150 patients, with a median number of four biopsies (range, 1-9) for each patient; protocol biopsies were 51 (median: one for each patient). In a median of 27 mo of follow up after OLT (range, 12-66mo), eight patients (8.8%; 6/8 were HCV positive) developed histological cirrhosis. The causes of cirrhosis in the two HCV negative patients were severe *de novo* autoimmune hepatitis and *de novo* HBV infection, respectively. At completion of the first post-transplant year, the median SFP was significantly faster in HCV positive in comparison to HCV-negative recipients: 0.083 (range, 0-0.455) *vs* 0.059 (range, 0-0.250) FU/mo ($P<0.02$). Table 2 shows the associations observed between 1 year post-OLT SFP >0.100 FU/mo and clinical and demographic characteristics of patients. Older donor age and lower BMI value pre-OLT were both significantly associated with faster fibrosis progression in HCV positive but not in HCV-negative recipients.

Figure 1 shows the fibrosis progression rates calculated at 1-4 years after OLT in the HCV-positive recipients. The fastest rate of fibrosis progression was observed during the 1st year after OLT. Later biopsies demonstrated a decrease in SFP with a non linear logarithmic trend ($r = 0.436$, $F = 37.1$, $P<0.0001$). Starting with the 3rd year after OLT, the SFP stabilized. Among the variables reported in Table 2, only a BMI value 1 year post-OLT >27.5 kg/m^2 was significantly associated with fibrosis progression <0.050 FU/mo (8/8 *vs* 18/35; $P<0.02$) in the 2nd year post-OLT. There was no difference in the SFP at 1 and 2 years post-OLT between patients that completed antiviral therapy as scheduled in comparison to those that either were untreated or terminated early interferon plus ribavirin treatment.

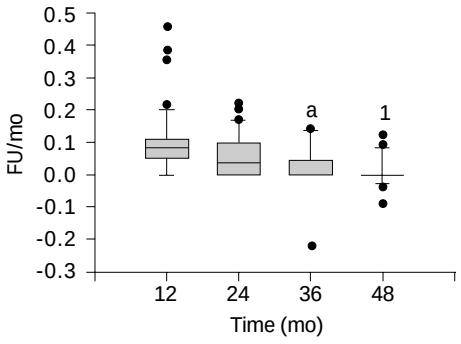

Figure 1 Vertical box plots of fibrosis progression rates in HCV-positive recipients, expressed as FU/mo, at different time points after the transplant operation. Median values, 10th, 25th, 75th, and 90th percentile are reported. Dots indicate outliers. [a]$P<0.005$ in comparison to FU/mo at 12 mo (Wilcoxon matched pairs signed rank sum test), [1]$P = 0.0001$ in comparison to FU/mo at 12 mo (Wilcoxon matched pairs signed rank sum test).

To further explore the relationship between gender and BMI, on the one hand, and fibrosis progression, on the other,

Table 2 Frequencies of patients with a SFP ¡Ý0.100 FU/mo in the 1st year post-OLT, in relationship with a selection of demographic and clinical variables

	All patients ($n = 90$) FU/mo ¡Ý0.100 $n = 70$	HCV-positive patients ($n = 55$) FU/mo ¡Ý0.100 $n = 39$	HCV-negative patients ($n = 35$) FU/mo ¡Ý0.100 $n = 31$
Recipient male gender ($n = 63$)	53[a]	29	24
Donor male gender ($n = 53$)	40	19	21
Recipient age ¡Ý55 yr ($n = 54$)	42	19	23
Donor age ¡Ý45 yr ($n = 54$)	47[d]	29[f]	18
Pre-OLT BMI >26.0 kg/m^2 ($n = 35$)	32[b]	16[c]	16
Tacrolimus therapy ($n = 69$)	56	31	25
Corticosteroid tapering >90 d ($n = 47$)	39	25	14
Diabetes mellitus ($n = 24$)	17	10	7

FU/mo: fibrosis units per month, HCV: hepatitis C virus, BMI: body mass index, [a]$P<0.05$ *vs* recipient female gender, [b]$P<0.02$ *vs* pre-OLT BMI ¡Ý26 kg/m^2, [d]$P<0.01$ *vs* donor age >45 yr; [c]$P<0.05$ *vs* pre-OLT BMI ¡Ý26 kg/m^2, [f]$P<0.001$ *vs* donor age >45 yr. P value refers to χ^2.

Table 3 Degree of hepatic steatosis in 105 biopsies performed between 12 and 36 mo after the transplant operation (HCV-positive recipients only), in relationship with a selection of variables

	Steatosis			
	Absent (n = 34)	¡Ü10% (n = 60)	>10% (n = 11)	P
Ishak staging score ¡Ü2 (n = 79)	19	49	11	<0.005
Recipient male gender (n = 72)	20	42	10	<0.05
Recipient age ¡Ü55 yr (n = 50)	15	28	7	NS
Donor age ¡Ü45 yr (n = 65)	19	39	7	NS
BMI increase <1.5 kg/m^2 (n = 76)	29	41	6	<0.05
Recurrent hepatitis C ¡Ü1 yr post-OLT (n = 79)	31	41	7	<0.02
Diabetes mellitus (n = 31)	10	18	3	NS

BMI: body mass index, OLT: orthotopic liver transplantation, BMI increase: difference between BMI value 1 yr post-OLT and BMI value pre-OLT. P value refers to χ^2 for linear trend.

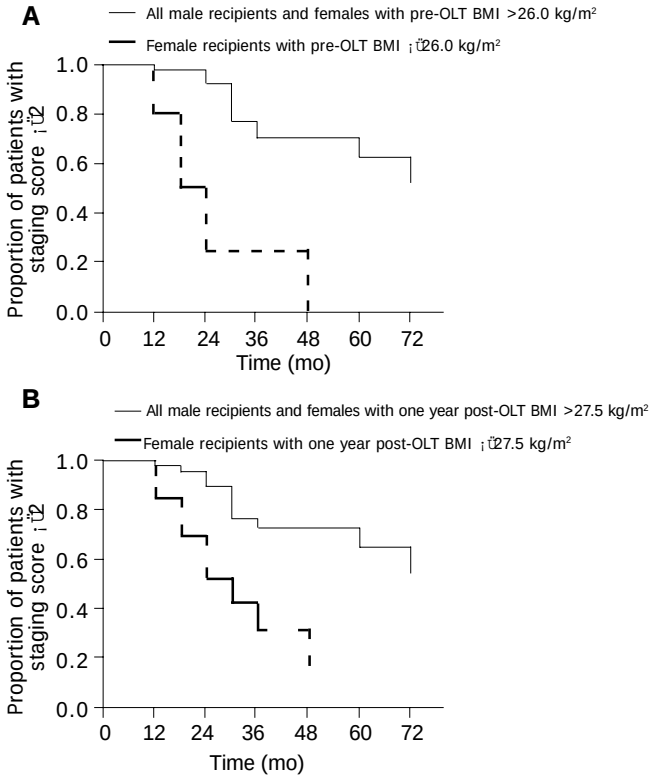

Figure 2 A: Time-to-event analysis to reach a staging score >2. HCV-positive recipients were divided as follows: all the male recipients and those females with pre-OLT BMI value >26.0 kg/m^2 (n = 45, continuous line); females with pre-OLT BMI value ¡Ü26.0 kg/m^2 (n = 10, dotted line). B: Time-to-event analysis to reach a staging score >2. HCV-positive recipients were divided as follows: all the male recipients and those females with 1 year post-OLT BMI value >27.5 kg/m^2 (n = 42, continuous line); females with 1 year post-OLT BMI value ¡Ü27.5 kg/m^2 (n = 13, dotted line).

we categorized OLT recipients as follows: females with BMI pre-OLT ¡Ü26.0 kg/m^2 (group A^{pre}) or ¡Ü27.5 kg/m^2 1 year post-OLT (group A^{post}); males with pre-OLT BMI value ¡Ü26.0 kg/m^2 (group B^{pre}) or ¡Ü27.5 kg/m^2 1 year post-OLT (group B^{post}); recipients of either gender and pre-OLT BMI >26.0 kg/m^2 (group C^{pre}) or >27.5 kg/m^2 1 year post-OLT (group C^{post}). Group A^{pre} showed the fastest SFP 1 year post-OLT, in comparison to group B^{pre} and group C^{pre} (7/10 *vs* 7/27 *vs* 16/18; P<0.002 for linear trend); a similar trend also was found considering 1 year post-OLT BMI and 2 years post-OLT fibrosis progression (A^{post} 6/10 *vs* B^{post} 11/25 *vs* C^{post} 8/8; P<0.02 for linear trend). Time-to-event analysis showed that, in females with lower BMI, the probability to reach a staging score >2 was the highest in comparison to all other recipients; this observation held true either considering BMI values pre-OLT (Figure 2A, Mantel-Cox, P<0.0001) or BMI values 1 year after OLT (Figure 2B, Mantel-Cox, P = 0.0005). Stepwise logistic regression analysis was performed among the predictive variables that, at univariate analysis, were associated, with a P value <0.10, to faster SFP (donor age, recipient gender, type of immunosuppressive therapy, and pre-OLT BMI). A SFP in the 1st year post-OLT >0.100 FU/mo was independently associated with older donor age (improvement of χ^2 11.63, P = 0.001), female recipient gender (improvement of χ^2 5.09, P<0.05) and lower pre-OLT BMI value (improvement of χ^2 4.26, P<0.05).

Post-OLT BMI, blood lipids, and liver steatosis One year post-OLT, having a BMI >26.5 kg/m^2, was found to be associated with a triglycerides/cholesterol (T/C) ratio ¡Ü1 (14/15 *vs* 26/40, P<0.05). In relationship to the recipient gender, a low T/C ratio, i.e., higher serum levels of cholesterol than of triglycerides, was associated both to a delayed (>1 year) hepatitis C recurrence and to a slower post-OLT SFP. Female recipients with a high T/C ratio had the highest proportion of early hepatitis C recurrence and 1 year SFP >0.100 FU/mo, followed by male recipients with high T/C ratio and patients of either gender with low T/C ratio: 4/4 *vs* 11/11 *vs* 28/40 (P<0.05 for linear trend), and 4/4 *vs* 3/11 *vs* 9/40 (P<0.01 for linear trend), respectively.

One-hundred and five liver biopsies were performed in HCV-positive patients along the period of time elapsed between 12 and 36 mo post-OLT. Table 3 shows the relationship between hepatic steatosis and a selection of variables, including the Ishak fibrosis score. Male gender, delayed hepatitis C recurrence, and body weight gain post-OLT were positively associated with steatosis; on the contrary, progression to significant fibrosis was less frequent in the presence of hepatic steatosis.

DISCUSSION

Post-OLT fibrosis progression in patients transplanted for HCV-related liver cirrhosis has been recently reported to behave not linearly[15], reaching, a sharp increase in the first

2 years, a plateau at the 3rd year after OLT. In the present paper, we confirmed this observation, showing that fibrosis progression during the 1st year after OLT is faster than that observed in the longer follow-up, when the process tends to slow down. Furthermore, early fibrosis progression in the grafts of HCV recipients is confirmed to be related to factors pertaining both to the donor and to the host. First and most importantly, fibrosis progression is affected by the age of donors, in agreement with previous work by several authors who considered an aged donor as the strongest predictor of fibrosis progression in patients with post-OLT HCV recurrence[16]. Second, a novel finding and the focus of the present investigation, early fibrosis progression after OLT appears to be related to the BMI value measured either pre-OLT or post-OLT. The association is not direct, as one might expect, but inverse: the higher the BMI value, the lower is the degree of early fibrosis development. This association is peculiar to HCV-positive patients and was not observed in HCV-negative recipients. Third, the presence of steatosis in the graft, which occurs in association with the increase in BMI, does not predict, as reported in immune-competent patient, a higher fibrosis score. To reconcile these findings with the existing literature, the elements that need to be considered in detail concern the differences that exist between the natural history of HCV infection in immune-competent *vs* OLT patients, and the putative molecular mechanisms of HCV re-infection.

Obesity[5,8,9] and liver steatosis[6,17,18] are recognized factors of liver fibrosis progression in HCV-positive immune-competent patients. Some authors have hypothesized a direct steatogenic effect of HCV, supported by several lines of evidence: the development of progressive hepatic steatosis in transgenic mice expressing the HCV core gene[19], the inhibition of very low density lipoprotein (VLDL) secretion in a transgenic murine model expressing HCV core protein[20], the close relationship between intra-hepatic HCV RNA and development of steatosis[21], and the correlation between hepatic steatosis and hepatic HCV replication in patients infected with HCV genotype 3[22]. Others have investigated the mechanisms involved in the progression of liver fibrosis due to the concomitant presence of steatosis and HCV infection, suggesting that steatosis might contribute to fibrosis through a steatohepatitis-like pathway involving stellate cell activation and peri-sinusoidal fibrosis production[23]. In OLT patients, however, the situation is different. A recent report[24], while confirming that body weight is the best predictor of liver steatosis 12 mo post-OLT, demonstrated that allograft steatosis does not predict the severity of HCV recurrence in HCV-infected patients within the first 12 mo after OLT. The present results converge in the same direction, and suggest, for the first time, that overweight, while facilitates liver steatosis, on the other hand may protect the liver graft, during an initial phase, from the damage due to HCV recurrence. Further data outline the need to be cautious when transposing the information concerning the natural history of HCV in immune-competent patients to the natural history of HCV recurrence post-OLT. For example, female gender, known to be protective against fibrosis in immune-competent patients[25], is on the contrary a negative prognostic factor in the post-OLT setting[26]. The present data showed that, among the patients with the lowest BMI values, female recipients had a SFP faster than the corresponding males. Therefore, one might hypothesize that the stronger susceptibility of female recipients to HCV recurrence could be related, at least in part, to factors affected by the interrelationship between gender and BMI variations, for example the lipid profile.

According to recent studies, several aspects of HCV infection are connected with lipid metabolism and lipid profile modifications. Binding of HCV to cell membrane of hepatocytes is thought to occur via two putative HCV receptors: CD81, a cellular surface protein belonging to the tetraspanin protein super-family, and the low density lipoprotein receptor (LDL-r)[27-29]. The HCV envelope glycoprotein E2 may interact with the CD81 molecule, while HCV or HCV-LDL complexes interact preferentially with the LDL-r[30]. HCV circulates in blood in association with different lipoproteins: early in the course of the infection, the preferential association is with LDL, while later on the association is with high-density lipoproteins (HDL). In accordance, patients with immune-deficiencies present higher HCV RNA titers in the LDL and HDL fractions than the immune-competent counterparts[31]. During the early viremic phase of experimental HCV infection, several genes associated with lipid metabolism are upregulated; interestingly, the fatty acid synthesizing gene is expressed at higher levels among chimpanzees that attain sustained clearance of the virus[32]. Binding and internalization of HCV RNA containing particles seem strictly regulated by lipoproteins: an increase of LDL and other lipoproteins decreases the LDL-r HCV particles interaction[28,33,34] while an upregulation of the LDL-r increases the internalization of HCV[35]. According to a recently proposed model, virions are released by liver cells and may infect other liver cells via LDL-r; free β-lipoproteins may regulate the rate of the infection of liver cells by competing with the virus[29]. Considering altogether these observations, it is tempting to speculate that a particular lipid profile could be associated with a slower kinetic of HCV infection of the hepatocytes and as a consequence a lesser fibrosis progression of the graft. We calculated the ratio between serum triglycerides and serum cholesterol as a proxy index of the balance between VLDL and LDL in the circulation. An association was found between a low T/C ratio and a higher BMI 1 year post-OLT. As previously observed considering the association between BMI and fibrosis progression, the relationships between the value of T/C ratio and both the timing of hepatitis C recurrence and the 1 year fibrosis progression rate were gender-related: females with higher T/C ratio were found to present the fastest SFP. Following this line, one might hypothesize that a low BMI, especially for female patients, could be associated with a lipid profile characterized by reduced serum LDL/VLDL levels. In fact, the relationship between increasing body weight and blood lipid profile is stricter in men than in women[36-38]. Furthermore, we have previously found that recipient's carriage of at least one ε4 allele of the apo-lipoprotein E (an allelic variant associated with higher cholesterol levels) was associated with better histological outcome of recurrent hepatitis C in male, but not in female recipients[39]. An unfavorable lipoprotein profile could possibly enhance HCV infectivity through an

upregulation of LDL-r[40], or decreased interference of LDL at the level of the interaction between HCV and LDL-r[29].

In conclusion, post-OLT overweight in HCV-positive recipients does not represent a factor favoring early liver fibrosis development and could even be protective against it. The explanation of this unexpected finding might reside on the peculiar lipid profile of patients with excess body weight post-OLT, capable to modulate the severity of HCV recurrence and hence the speed at which liver fibrosis develops.

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