Liver Transplantation in Cirrhotic Patients With Diabetes Mellitus: Midterm Results, Survival, and Adverse Events

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Liver cirrhosis is frequently associated with diabetes mellitus (DM), and this metabolic complication is also frequent after orthotopic liver transplantation (OLT). The aim of our study is to investigate which factors are associated with DM before and after OLT and their impact on post-OLT evolution. We evaluated the prevalence of DM among 115 liver transplant candidates with cirrhosis and assessed their evolution after OLT (median follow-up, 41 months). Sixteen candidates had DM requiring pharmacological therapy (group A), 45 candidates had DM controlled with diet (group B), and 54 candidates did not have DM (group C). One-year and 3-year actuarial survival rates were 100% and 100% for group A, 91% and 85% for group B, and 77% and 74% for group C, respectively ($P < .03$). Post-OLT DM was more frequent in group A. The incidence of other metabolic complications, major infections, rejection, and arterial hypertension; the need for hospitalization; and renal and graft function of patients in groups A, B, and C were similar. The only risk factor for DM 1 year after OLT on multivariate analysis was pre-OLT DM requiring pharmacological treatment. The incidence of complications, need for hospitalization, and renal and graft function 1 year after OLT for patients with post-OLT DM were similar to those of patients without post-OLT DM. In conclusion, patients with cirrhosis who have DM have a greater risk for post-OLT DM, but their midterm survival is not worse than the survival of those without DM. (*Liver Transpl 2001;7:226-233.*)

Liver cirrhosis is frequently associated with impaired glucose metabolism.[1-3] Insulin resistance has been found in most patients with cirrhosis.[4-6] It seems to be caused mainly by a deficiency in insulin-stimulated glycogen synthesis in the muscle.[4] This insulin resistance increases the demand for pancreatic insulin secretion and may lead to overt diabetes mellitus (DM),[7] found in 10% to 30% of the patients with cirrhosis.

Glucose intolerance and insulin resistance of patients with cirrhosis are reversed after orthotopic liver transplantation (OLT),[8] but the use of such immunosuppressive drugs as cyclosporine, tacrolimus, or prednisone can alter glucose metabolism either by direct effect on pancreatic β-cells or by contributing to insulin resistance.[9-11] Thus, the global effect of OLT on glucose metabolism may be both prodiabetogenic and antidiabetogenic.

Some studies have reported the evolution of transplant recipients with DM after OLT.[12-17] In 1 study,[13] liver transplant recipients with DM had a lower survival rate than those without DM. Conversely, other studies did not show a difference between patients with and without DM.[12,14-17] In these studies, DM had been diagnosed according to serum fasting glucose levels, probably underestimating the incidence of liver cirrhosis–related DM.

The aim of this study is to investigate the prevalence of pre-OLT DM in end-stage liver cirrhosis and assess the evolution of patients with DM after OLT. In addition, factors predisposing to post-OLT DM were studied.

Patients and Methods

Study Design and Population

From February 1990 to October 1998, a total of 115 adult patients with liver cirrhosis undergoing OLT at a single institution were studied before OLT by means of an oral glucose tolerance test (OGTT) to rule out DM, unless they had a previous reported diagnosis of DM. According to the 1997 recommendations of the American Diabetes Association,[18] DM was diagnosed if fasting serum glucose levels were greater than 126 mg/dL or serum glucose concentrations were greater than 200 mg/dL 120 minutes after an OGTT using 75 g of anhydrous glucose. Impaired glucose tolerance was diagnosed when serum glucose levels were between 140 and 200 mg/dL 120 minutes after OGTT.

After DM was diagnosed, a diet avoiding simple sugars and limiting carbohydrate to 4 g/kg/d and regular exercise

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1527-6465/01/0703-0006$35.00/0
doi:10.1053/jlts.2001.22183

were recommended. If these measures were not sufficient to get good metabolic control, drug therapy (oral hypoglycemic agents or insulin) was initiated. Patients were divided into 3 groups: patients with DM requiring treatment other than diet and exercise (insulin or oral hypoglycemic agents) for control of DM (group A): patients with DM without need of pharmacological treatment (group B), and patients without DM (group C). None of the liver transplant recipients with DM had clinical, electrocardiographic, or echocardiographic findings suggestive of ischemic cardiac disease, major cerebrovascular disease (not including asymptomatic lacunar infarcts), advanced renal insufficiency, disabling peripheral neuropathy, or vasculopathy.

Post-OLT Patient Management

Immunosuppression consisted of a triple-drug regimen including cyclosporine or tacrolimus, azathioprine, and steroids. Before 1996, cyclosporine was administered intravenously (2 mg/kg twice daily) in the immediate postoperative period and was switched to the oral route. From 1996, therapy with oral cyclosporine microemulsion (5 mg/kg twice daily) was started in the immediate postoperative period. Patients administered tacrolimus were treated initially with 0.05 mg/kg orally twice daily. Cyclosporine and tacrolimus doses were adjusted according to blood trough levels. Patients on cyclosporine therapy were administered 1,000 mg of intravenous methylprednisolone intraoperatively, followed by a tapering schedule of 200 to 20 mg/d in the first 6 postoperative days. Patients treated with tacrolimus were administered 5 mg/kg of methylprednisolone intraoperatively and in the first postoperative day, reduced to 20 mg/d on postoperative day 2. Prednisone dosage was slowly reduced, and its withdrawal was attempted 12 to 24 months after OLT from 1990 to 1996 and 6 to 12 months after OLT from 1997 to 1998. Azathioprine was administered at a dose of 1 to 2 mg/kg/d and adjusted according to hematologic tolerance. After steroid withdrawal, azathioprine dosage was slowly reduced until it was discontinued. Mild episodes of graft rejection were treated with an increase in cyclosporine or tacrolimus dose. Those patients who did not respond to this change in therapy or those with moderate or severe rejection were treated with a short course of high-dose steroid therapy (methylprednisolone, 1,000 mg/d intravenously for 3 days), followed by a 6-day tapering dosage (methylprednisolone from 200 to 20 mg/d intravenously).

All patients were administered systemic perioperative antibiotic prophylaxis with amoxicillin/clavulanate for 2 days and oral administration of norfloxacin, cloxacillin, and nystatin for 4 to 6 days.

After discharge, patients were regularly followed up by staff members of the liver transplant unit every week for the first month, every 15 days for the next 3 months, and then every month for the first year. If there were no complications, subsequent follow-up was every 3 months thereafter.

The OGTT was not repeated after OLT; therefore, post-OLT DM was defined as the need for pharmacological treatment (insulin or oral antidiabetic agents) to maintain normal glucose levels before and after meals and a glycosylated hemoglobin level less than 6.2%. Hypercholesterolemia was diagnosed if fasting serum cholesterol levels were greater than 250 mg/dL in the absence of lipid-reducing therapy. Hypertriglyceridemia was defined as a fasting serum triglyceride level greater than 170 mg/dL. Obesity was defined as a body mass index (BMI) greater than 30 kg/m^2 and overweight as a BMI between 27 and 30 kg/m^2. Arterial hypertension was defined as a diastolic blood pressure greater than 90 mm Hg and/or a systolic blood pressure greater than 140 mm Hg. Major infection was defined as a positive culture from blood or deep tissue associated with the presence of sepsis syndrome.

Data Collection

All patients were followed up until March 1999. Medical records were retrospectively analyzed for each patient in the 3 groups. The possible relationship between DM and several pre-OLT variables was analyzed. These variables were age, sex, blood group, BMI, cause of liver cirrhosis, association with hepatocellular carcinoma, standard renal and liver function tests, Child-Pugh status, antidiabetic treatment, HLA-DR3 and -DR4 antigens, arterial hypertension, hypertriglyceridemia, and hypercholesterolemia.

To assess the possible influence of DM on post-OLT outcome, survival was compared among groups A, B, and C. The incidence of DM, obesity, hypercholesterolemia, hypertriglyceridemia, and arterial hypertension at 3 months and 1, 2, and 3 years in each group were recorded. The incidence of major infections and rejection episodes during the first year post-OLT in the 3 groups was compared. In addition, the length of hospitalization until intensive care unit and hospital discharge and in the first post-OLT year were compared among the 3 groups. Standard hepatic and renal function test results were also studied during the 3 years of follow-up.

To assess which factors could predispose to post-OLT DM, patients with and without post-OLT DM 1 year after OLT were compared. Pre-OLT variables analyzed were age, sex, blood group, HLA-DR3 and -DR4, incidence of overweight or obesity, Child-Pugh status, cause of liver cirrhosis, presence of hepatocellular carcinoma, hypercholesterolemia, arterial hypertension, and standard renal and liver function test results. Post-OLT variables analyzed were daily and cumulative steroid doses, immunosuppression with cyclosporine or tacrolimus, cyclosporine levels, and incidence of rejection episodes in the first year post-OLT. The possible influence of tacrolimus levels on the incidence of post-OLT DM was not studied because of the low number of patients administered tacrolimus in this series.

The possible influence of post-OLT DM on the evolution of the patients was assessed by comparing the incidence of rejection and major infections during the first year post-OLT; arterial hypertension, hypertriglyceridemia, and hypercholesterolemia at the end of the first year post-OLT; serum levels of

albumin and creatinine; prothrombin ratio; and days of hospitalization required in the intensive care unit, before hospital discharge, and in the first year.

Statistical Analysis

Statistical analyses were performed using SPSS for Windows release 9.0.1 (SPSS Inc, Chicago IL). Comparisons of 2 series of numerical variables were performed with the Mann-Whitney *U* test. When more than 2 series of continuous variables were compared, the Kruskal-Wallis test was used, and if $P < .05$, comparisons between groups were performed with the Mann-Whitney *U* test and Bonferroni adjustment was finally applied. Categorical data were compared by Chi-squared test using Fisher's correction if indicated.

For analysis of predisposing factors for the development of post-OLT DM, those variables showing *P* less than .20 were included in a multivariate logistic regression model to determine which factors were independently associated with this complication. The goodness of fit of the model was assessed with the Hosmer-Lemeshow test.

Actuarial patient and graft survival rates were estimated by means of the Kaplan-Meier method and compared by means of the log-rank test.

Significance was established at $P < .05$. Continuous variables are expressed as mean ± SEM.

Results

Patient Characteristics

Before OLT, 25 patients (22%) had a normal OGTT result, 29 patients (25%) had impaired glucose tolerance, and 61 patients had DM. In only 19 of 61 patients had DM been diagnosed before referral for OLT. Pharmacological treatment was required in 16 of 61 patients with diabetes (26%; group A). Ten of these patients required insulin (34.10 ± 4.34 UI/d); none had DM type 1 or signs of chronic pancreatitis. Group B consisted of 45 patients (39%) with DM who required only diet and physical exercise, and group C consisted of 54 patients (47%) without DM.

Pre-OLT demographic, clinical, and laboratory data from these 3 groups of patients are listed in Table 1. As expected, fasting serum glucose levels were significantly greater in patients in group A than in patients in groups

Table 1. Pre-OLT Demographic, Clinical, and Laboratory Data From 115 Liver Transplant Recipients

	Group A (n = 16)	Group B (n = 45)	Group C (n = 54)	*P*
Age (yr)	54.9 ± 2.0	56.0 ± 1.2	54.1 ± 1.3	NS
Sex				.004
Men	16 (100)	30 (67)	39 (72)	
Women	0 (0)	15 (33)	15 (28)	
BMI				NS
Normal	8 (50)	29 (64)	30 (55)	
Overweight	6 (37)	9 (20)	16 (30)	
Obese	2 (13)	7 (16)	8 (15)	
Etiology of liver cirrhosis				NS
Alcoholic liver disease	10 (62)	12 (27)	22 (41)	
Hepatitis C virus	4 (25)	17 (38)	18 (33)	
Other	2 (13)	16 (35)	14 (26)	
Child-Pugh stage				NS
A	3 (19)	5 (11)	8 (15)	
B	7 (44)	27 (60)	25 (46)	
C	6 (37)	13 (29)	21 (39)	
HCC	6 (37)	14 (31)	13 (24)	NS
Arterial hypertension	1 (6)	4 (9)	4 (7)	NS
Hypercholesterolemia	1 (6)	1 (2)	5 (9)	NS
Hypertriglyceridemia	1 (6)	0 (0)	1 (2)	NS
Glucose (mg/dL)	137.8 ± 12.1	95.1 ± 3.3	82.1 ± 1.5	<.001*
Albumin (g/dL)	2.92 ± 0.14	2.96 ± 0.09	2.90 ± 0.07	NS
Prothrombin rate (%)	62 ± 3	59 ± 2	64 ± 3	NS

NOTE. Group A, DM with pharmacological treatment; group B, DM without pharmacological treatment; group C, no DM. Values expressed as mean ± SEM or number (percent).
Abbreviations: HCC, hepatocellular carcinoma; NS, not significant.
* Comparisons between all groups (A *v* B, A *v* C, B *v* C), $P < .005$.

B and C. There was a significant difference among groups: all patients in group A were men. The rest of the variables studied were not significantly different among groups.

Survival

Patients were followed up for a median of 41 months (range, 4 to 99 months). At the end of follow-up, 21 patients had died after OLT (0 patients, group A; 6 patients, group B; 15 patients, group C). Actuarial survival rates 1, 3, and 5 years after OLT were 86%, 82%, and 80% for the whole series; 100%, 100%, and 100% in group A; 91%, 85%, and 85% in group B; and 77%, 74%, and 71% in group C. Actuarial survival curves are shown in Figure 1. As noted, the difference in survival reached statistical significance.

Evolution After OLT

As listed in Table 2, there were no significant differences among the 3 groups in the incidence of acute rejection or major infections or the mean number of hospitalization days required in the intensive care unit, before post-OLT discharge, or in the first post-OLT year. Serum albumin and creatinine levels and prothrombin activity were similar among the 3 groups, as were mean cumulative and daily doses of prednisone.

Table 3 lists the incidence of metabolic complications in the 3 groups of patients. There were no differences in the incidence of post-OLT arterial hypertension, hypercholesterolemia, hypertriglyceridemia, or overweight or obesity among the 3 groups. The incidence of post-OLT DM 3 months and 1, 2, and 3 years after OLT was significantly greater in group A than in groups B and C. The incidence of DM in group B was greater than that in group C 3 months and 1 year after OLT, but this difference disappeared by 2 years.

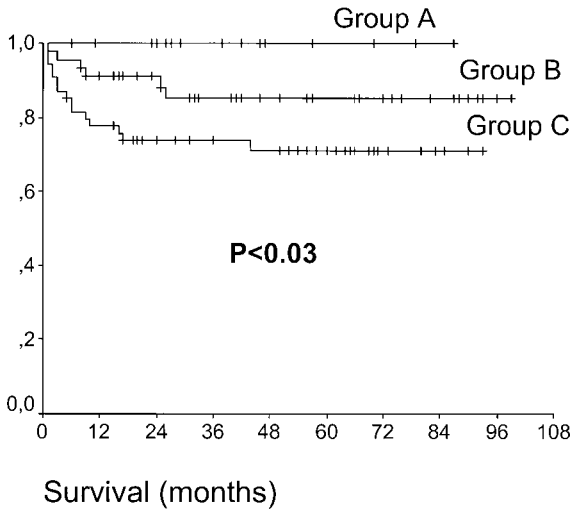

Figure 1. Actuarial survival after OLT in patients with pre-OLT DM requiring (group A) or not requiring (group B) pharmacological treatment and in patients without DM (group C).

Prevalence and Risk Factors for Post-OLT DM

Ninety-two patients were followed up for more than 1 year after OLT. Twenty-four of these patients had DM at that time; 22 patients (24%) required insulin therapy (25.41 ± 12.15 UI/d) and 2 patients required oral antidiabetic therapy to maintain good metabolic control. Among the variables investigated, history of pre-OLT DM and incidence of hepatocellular carcinoma showed *P* less than .2 on univariate analysis (Table 4). On multivariate analysis, only pre-OLT DM requiring treatment was predictive of post-OLT DM. Taking group C as the reference stratum, the odds ratios for DM 1 year after OLT were 3.72 (95% confidence interval, 0.92 to 15.08; $P = .066$) for group B and 72 (95% confidence interval, 11 to 490; $P < .0001$) for group A. *P* for Hosmer-Lemeshow test for goodness of fit was .63.

Consequences of Post-OLT DM

Post-OLT evolutions of patients who did or did not have DM 1 year after OLT were compared (Table 5). Both groups were similar in the incidence of acute rejection, major infections, overweight or obesity, arterial hypertension, hypertriglyceridemia, and hypercholesterolemia. Days of hospitalization in the intensive care unit, global hospitalization before discharge, and cumulative 1-year hospitalization were also similar. Creatinine and albumin levels and prothrombin activity were also similar in both groups.

Discussion

Glucose intolerance is a very frequent finding in patients with end-stage liver cirrhosis. This is mainly caused by insulin resistance and leads to overt DM in 10% to 30% of patients. In this report, we found a prevalence of DM greater than 50% in liver transplant candidates with liver cirrhosis in contrast to its lower incidence in other series.[12-17] A factor that may contribute to this difference is the low proportion of patients with cholestatic liver disease in our series compared with others. Zein et al[16] found a lower prevalence of DM in patients with chronic cholestasis than in those with liver cirrhosis caused by hepa-

Table 2. Comparison of Post-OLT Data of Patients

	3 Months	1 Year	2 Years	3 Years
Group A				
No. of patients	16	14	11	7
Creatinine (mg/dL)	1.14 ± 0.09	1.39 ± 0.14	1.53 ± 0.16	1.31 ± 0.07
Cumulative prednisone dose (mg)	4,285 ± 481	7,417 ± 816	10,134 ± 1,083	13,237 ± 2,254
Current prednisone dose (mg/d)	16.40 ± 1.51	6.43 ± 1.25	5.23 ± 1.14	5.00 ± 2.11
Cyclosporine level (ng/mL)	224 ± 27	183 ± 19	146 ± 33	120 ± 28
Rejection episodes		4/16 (31)		
Major infections		3/16 (19)		
Days in intensive care unit	5.31 ± 0.39			
In-hospital days	18.63 ± 9.62	34.36 ± 3.9		
Group B				
No. of patients	44	38	29	23
Creatinine (mg/dL)	1.12 ± 0.04	1.15 ± 0.05	1.29 ± 0.06	1.30 ± 0.06
Cumulative prednisone dose (mg)	4,992 ± 422	8,905 ± 700	13,382 ± 891	16,984 ± 1,117
Current prednisone dose (mg/d)	17.60 ± 0.61	9.37 ± 1.01	6.80 ± 0.87	5.72 ± 0.99
Cyclosporine level (ng/mL)	239 ± 14	193 ± 9	150 ± 12	129 ± 11
Rejection episodes		17/45 (38)		
Major infections		14/45 (31)		
Days in intensive care unit	7.14 ± 0.61			
In-hospital days	25.41 ± 2.63	50.90 ± 5.17		
Group C				
No. of patients	47	40	31	26
Creatinine (mg/dL)	1.29 ± 0.11	1.36 ± 0.14	1.35 ± 0.08	1.35 ± 0.06
Cumulative prednisone dose (mg)	4,827 ± 338	8,338 ± 517	11,993 ± 594	15,048 ± 612
Current prednisone dose (mg/d)	17.87 ± 0.58	8.94 ± 0.90	6.08 ± 0.58	4.61 ± 0.53
Cyclosporine level (ng/mL)	251 ± 16	190 ± 12	153 ± 11	135 ± 10
Rejection episodes		16/54 (30)		
Major infections		15/54 (28)		
Days in intensive care unit	6.78 ± 0.61			
In-hospital days	28.72 ± 2.84	50.90 ± 5.57		

NOTE. Group A, DM with pharmacological treatment; group B, DM without pharmacological treatment; group C, no DM. Values expressed as mean ± SEM or number of patients/total number (percent). All comparisons are between groups and not significant.

titis C or alcohol. In our series, 0 of the 7 patients with chronic cholestasis had DM (and only 1 patient had impaired glucose tolerance) compared with 22 of 44 patients with alcoholic liver disease and 21 of 39 patients with cirrhosis caused by hepatitis C. This different prevalence is highly significant, but its value is limited because of the low number of patients with chronic cholestasis.

The most important reason for this difference between our study and others is the different criteria used for the diagnosis of DM. Previous studies had defined DM as fasting plasma glucose levels greater than 140 mg/dL. In our study, according to the proposal of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus,[18] the diagnosis of DM was established for fasting plasma glucose levels greater than 126 mg/dL or plasma glucose levels greater than 200 mg/dL after an OGTT, confirming these results in a second determination on a separate day. Most diagnoses of DM were based on the OGTT. Only 7 of 61 patients (11%) with DM had fasting plasma glucose levels greater than 140 mg/dL. Even if the threshold for the diagnosis of DM is decreased to 126 mg/dL, only 12 of 61 patients (20%) are correctly diagnosed with DM. Using the criteria used in other reports, the prevalence of DM in our liver transplant recipients was the same as that in other series.

When we studied which factors are related to liver cirrhosis–associated DM, the only difference was the greater prevalence of DM requiring pharmacological treatment in men. We did not find a difference among groups with respect to age, blood group, prevalence of HLA-DR3 or -DR4 antigens, incidence of overweight or obesity, cause of liver disease (excluding chronic cho-

Table 3. Post-OLT Incidence of DM, Obesity, Hypercholesterolemia, Hypertriglyceridemia, and Arterial Hypertension

	3 Months	1 Year	2 Years	3 Years
Group A				
No. of patients	16	14	11	7
DM	14/16 (87)*,†	12/14 (86)*,†	9/11 (82)*,†	4/7 (57)*,†
BMI				
Normal	9/15 (60)	3/13 (23)	2/10 (20)	0/6 (0)
Overweight	3/15 (20)	6/13 (46)	4/10 (40)	3/6 (50)
Obese	3/15 (20)	4/13 (31)	4/10 (40)	3/6 (50)
Hypercholesterolemia	6/16 (37)	3/14 (21)	4/11 (36)	2/7 (29)
Hypertriglyceridemia	3/16 (19)	6/14 (43)	6/11 (55)	3/7 (43)
Arterial hypertension	9/16 (56)	10/14 (71)	10/11 (91)	4/7 (57)
Group B				
No. of patients	44	38	29	23
DM	16/44 (36)*	9/38 (24)	3/29 (10)	2/23 (9)
BMI				
Normal	32/43 (74)	19/38 (50)	13/29 (45)	9/21 (43)
Overweight	7/43 (16)	8/38 (21)	5/29 (17)	2/21 (10)
Obese	4/43 (9)	11/38 (29)	11/29 (38)	10/21 (48)
Hypercholesterolemia	14/43 (33)	14/38 (37)	7/29 (24)	7/23 (30)
Hypertriglyceridemia	8/40 (20)	13/38 (34)	4/29 (14)	4/23 (17)
Arterial hypertension	27/44 (61)	25/38 (66)	21/29 (72)	18/23 (78)
Group C				
No. of patients	47	40	31	26
DM	1/47 (2)	3/40 (7)	1/31 (3)	1/26 (4)
BMI				
Normal	29/47 (62)	13/38 (34)	10/30 (33)	9/26 (35)
Overweight	8/47 (17)	10/38 (26)	8/30 (27)	7/26 (27)
Obese	10/47 (21)	15/38 (39)	12/30 (40)	10/26 (38)
Hypercholesterolemia	12/47 (26)	15/40 (37)	10/31 (32)	9/25 (36)
Hypertriglyceridemia	12/40 (30)	10/40 (25)	9/30 (30)	6/25 (24)
Arterial hypertension	20/47 (43)	30/40 (75)	24/31 (77)	21/26 (81)

NOTE. Group A, DM with pharmacological treatment; group B, DM without pharmacological treatment; group C, no DM. Values expressed as number of patients/total number (percent).
* $P < .005$ versus group C.
† $P < .02$ versus group B.

lestasis, as noted), incidence of hepatocellular carcinoma, and liver and renal function.

The most important finding of this report is the confirmation of the lack of an adverse outcome in liver transplant recipients with DM compared with patients without DM. Post-OLT survival of liver transplant recipients with DM had been reported to be less than the survival of those without DM in 1 series,[13] but the rest of the series reported to date did not find significant differences.[12,14-17] Our patients with DM had greater survival and it was even greater in those who required pharmacological treatment to achieve metabolic control. Excluding the incidence of post-OLT DM, the rest of the outcomes studied were not different among groups. We studied the incidence of rejection, major infections, and such metabolic complications as obesity and hyperlipidemia. In addition, graft (expressed as serum albumin levels and prothrombin time) and renal function (expressed as creatinine levels) were similar among groups. Most previous studies had found a similar incidence of complications in both groups. Only Trail et al[14] found a greater incidence of minor bacterial and fungal infections in patients with DM. These investigators also found that patients with pre-OLT DM had worse renal function in the first post-OLT year than patients without DM. In the same way, patients with and without post-OLT DM in our series had similar post-OLT evolutions. The good evolution of patients with pre-OLT DM after OLT must be interpreted cautiously because none of our patients had severe organ damage caused by pre-OLT DM.

The most important difference in the evolution of

Table 4. Predictive Factors for DM 1 Year After OLT

	No Post-OLT DM (n = 68)	Post-OLT DM (n = 24)	*P*
Pre-OLT			
Age (yr)	53.2 ± 9.8	55.7 ± 7.1	NS
Sex			NS
Men	49 (72)	20 (83)	
Women	19 (28)	4 (17)	
DM			<.001
No	37 (54)	3 (12)	
Without treatment	29 (43)	9 (38)	
With treatment	2 (3)	12 (50)	
Weight			NS
Normal	38 (56)	13 (54)	
Overweight	17 (25)	8 (33)	
Obese	13 (19)	3 (13)	
Child-Pugh stage			NS
A	10 (15)	3 (12)	
B	35 (51)	11 (46)	
C	23 (34)	10 (42)	
Hepatocellular carcinoma	16 (24)	9 (37)	.146
Hypercholesterolemia	5 (7)	1 (4)	NS
Arterial hypertension	5 (7)	3 (12)	NS
Post-OLT			
Weight			NS
Normal	28 (42)	7 (32)	
Overweight	15 (22)	9 (41)	
Obese	24 (36)	6 (27)	
Immunosuppression			NS
Cyclosporine A	60 (88)	22 (92)	
Tacrolimus	8 (12)	2 (8)	
Cyclosporine level (ng/mL)	194 ± 9	180 ± 11	NS
Cumulative prednisone (mg)	8,382 ± 477	8,575 ± 623	NS
Prednisone (mg/d)	8.87 ± 0.75	8.33 ± 0.95	NS

NOTE. Data expressed as mean ± SEM or number (%).
Abbreviation: NS, not significant.

patients with and without pre-OLT DM is the incidence of post-OLT DM. Most patients who required pharmacological treatment before OLT to achieve blood glucose control required treatment in the next years. Patients with pre-OLT DM not requiring treatment also had a greater incidence of post-OLT DM during the first year, but the difference between these patients and those without DM lost its significance later. Post-OLT DM was very infrequent in patients without DM before OLT, and none of the patients with normal OGTT results had post-OLT DM at any of the times studied (3, 12, 24, and 36 months). As shown, the incidence of post-OLT DM is greatest in the early post-OLT period, probably because of the greater doses of immunosuppressive drugs used during this period and the persistence of some degree of portasystemic shunting. None of the patients without DM at the end of the first year became diabetic later.

In their report, Navasa et al[12] found that the only factor predicting the development of post-OLT DM among patients without DM was rejection because the number of rejection episodes was greater in patients with than without post-OLT DM. In our series, the incidence of rejection in patients with and without post-OLT DM was similar, as were the rest of the variables studied. The only difference between both groups was the greater incidence of pre-OLT DM requiring treatment in patients who remain diabetics. There was also a clear trend to a greater incidence of DM 1 year after OLT in those patients who had pre-

Table 5. Comparison of the Evolution After OLT in Patients With and Without DM 1 Year After OLT

	No Post-OLT DM (n = 68)	Post-OLT DM (n = 24)	*P*
Weight			NS
Normal (%)	28 (42)	7 (32)	
Overweight (%)	15 (22)	9 (41)	
Obese (%)	24 (36)	6 (27)	
Arterial hypertension (%)	47 (69)	18 (75)	NS
Hypercholesterolemia (%)	24 (35)	8 (33)	NS
Hypertriglyceridemia (%)	19 (28)	10 (42)	NS
Rejection (%)	22 (32)	9 (37)	NS
Major infection (%)	17 (25)	4 (17)	NS
Hospitalization (d)			
ICU	7.01 ± 0.50	6.54 ± 0.57	NS
Until discharge	27.32 ± 2.44	25.25 ± 2.92	NS
1 Year (cumulative)	46.81 ± 3.79	52.88 ± 6.75	NS
Albumin (g/dL)	3.88 ± 0.05	3.79 ± 0.08	NS
Creatinine (mg/dL)	1.30 ± 0.09	1.22 ± 0.06	NS
Prothrombin rate (%)	93 ± 2	96 ± 3	NS

NOTE. Data expressed as mean ± SEM or number (percent).
Abbreviations: ICU, intensive care unit; NS, not significant.

OLT DM not requiring treatment. Similarly, Bigam et al[17] found that 1 of the predisposing factors for post-OLT DM is pre-OLT DM. Contrary to our findings, these investigators also found hepatitis C–related liver failure and male sex as independent predictors of DM 1 year after OLT.

A recent report from Italy may help explain these findings.[8] In their study, Perseghin et al found that patients with cirrhosis with DM may have insulin resistance and reduced β-cell function. The first of these 2 alterations is reversed after OLT, but reduced β-cell secretion is not. This reduced β-cell function probably has a key role in the maintenance of DM after OLT, making the development of DM almost exclusive of patients who have decreased insulin secretion before OLT.

In conclusion, patients with end-stage liver cirrhosis have a high prevalence of DM. This condition does not have an adverse consequence on morbidity and mortality other than the maintenance of their diabetic state. The only risk factor for the development of post-OLT DM is pre-OLT DM, but this complication does not have an adverse effect on midterm survival.

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