Donor Characteristics Associated with Liver Graft Survival

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Background. Organ availability is affecting the development of liver transplantation in its entirety, leading to transplant teams expanding the criteria for accepting organ donors. In these circumstances, analysis of the impact of the donor's characteristics on graft survival becomes mandatory.
Methods. Fifty-two donor variables from 5,150 liver transplants performed in Spain between 1994 and 2001 were analyzed through a univariate analysis. Those with statistically significant impact on graft survival were entered in a Cox regression model with the recipients' characteristics and other factors linked to the graft technique.
Results. Several donor factors negatively affect graft survival: donor age, cause of death, body mass index, vasoactive drug administration, prolonged intensive care unit (ICU) stay, increased alkaline phosphatase and liver enzyme levels, low bicarbonate level, and antecedents of hypertension. However, only four can be mentioned as representing a risk for losing the graft when donor variables are controlled with recipient or technique variables in a Cox regression model: donor age, antecedents of hypertension, prolonged ICU stay, and low bicarbonate level. In the same analysis, norepinephrine administration has a relative risk less than 1.
Conclusions. The multivariate analysis of the impact of 52 donor characteristics on liver graft survival showed the negative effect of an elderly donor, with hypertension combined with the presence of metabolic acidosis, or a prolonged ICU donor stay. The administration of norepinephrine alone during donor management showed a protective effect.

Keywords: Liver transplant, Liver donor, Graft survival.

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Liver transplantation is currently a usual therapeutic approach that has increased dramatically within the last years because of the positive results. The most important factor affecting the whole development of such therapies is the shortage of organs for transplantation. Even in the case of Spain with approximately 34 organ donors per million population and 25 liver transplants per million population/year (the highest organ donation or transplantation rates worldwide), annual mortality for those on the waiting list is approximately 10% (*1*). To face this organ shortage, transplant teams developed different alternatives (*2*). Among these alternatives we found the acceptance of so-called expanded donors. This led to an increased interest in the analysis of the impact of donor characteristics on graft survival (*3*).

Several factors have been identified to be associated with low graft survival and thus considered as risk factors. Among them are the following: elderly or female donor (*4–8*), especially in recipients with hepatitis C virus (HCV) (*9*, *10*) or male recipients, respectively (*11*, *12*); vasoactive drug treatment; cardiac arrest (*13*); sustained hypotension; prolonged stay in the intensive care unit (ICU) (*3*, *14*); viral or bacterial infectious diseases (*15*); altered biochemical data (hypernatremia or acidosis) (*8*, *14*); alcohol intake; and the presence of steatosis (*3*, *17*, *18*). However, it must be stated that most studies involve retrospective data analysis covering only partial aspects and usually few registered charts. There are great discrepancies among the published data and a lack of unanimity in relation to the statement and definition of risk factors.

Spanish organ donor characteristics changed in the last few years. In 1992, only 10% of donors were aged more than 60 years, whereas in 2003 this percentage was 34%, with 16.5% of the donors aged more than 70 years. The current average organ donor's age is approximately 50 years (*19*). Consequently, the number of grafts performed with the organs of elderly donors is high, giving us the opportunity to evaluate and control the exact impact that donor age has on graft survival, alone or in relation with other characteristics related to the donor, recipient, or surgical procedure.

MATERIALS AND METHODS

During 2002 and 2003, the National Organization of Transplants retrospectively reviewed the 5,150 liver grafts performed in patients aged more than 16 years in Spain between 1994 and 2001. Graft survival was analyzed in relation to the characteristics of the donor, recipient, and surgical procedure.

Donor data were collected from the National Organization of Transplants' donor registry database. A new entry is added to this donor registry every time a donor is referred to the office (all donors are referred to the office in due time for the allocation process to be carried out). Data include medical antecedents, clinical characteristics, biochemical data, complementary tests, received treatment, and hemodynamic parameters.

Data related to the recipient's characteristics, technical procedures, and graft evolution were obtained from the Spanish Liver Transplant Registry database.

Statistical Methodology

Descriptive statistical analysis included proportional tests for qualitative data and means and standard deviations

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for quantitative data. After that, univariate graft survival analysis was conducted with the life-table methodology. The Wilcoxon test was used to compare the different categories. Continuous variables were dichotomized for analysis at points empirically thought to have clinical relevance or using percentiles 75 or 90 as threshold values.

Finally, a Cox proportional hazard multivariate model for survival was computed using all variables with a significant statistical level ($P<0.10$) in the univariate analysis, as well as those considered medically relevant. Variables related to the recipient and the surgical procedure were introduced to control possible confusion factors and to know the exact weight of each variable on graft survival. Those variables were as follows: number of transplants, urgency status, ABO compatibility, sex compatibility, period of transplant performance, mean transplant activity in the center, ischemia time, perfusion liquid, bypass technique, associated transplants, recipient's age, severity status pretransplant of the liver recipient using United Network for Organ Sharing classification, recipient's primary disease, and presence or absence of HCV infection.

Furthermore, the proportionality of the variables' risks was studied, and the variables that did not meet the criteria were modified for the Cox analysis. For all obtained relative risks (RRs), we calculated the statistical significance and confidence interval at the 95% level.

All statistical analysis was performed using SPSS v.10 (SPSS Inc., Chicago, IL).

RESULTS

Descriptive Analysis of Donor Characteristics

Table 1 shows both qualitative and quantitative variables (52) from the donor analyzed in the 5,150 cases of liver transplant included in the study. Absolute numbers and proportions are shown for qualitative variables. Mean and standard deviation are presented for quantitative variables. Most donors were male (63%) with an average age of 45 years. The main cause of death was a stroke, and approximately 25% were hypertensive with a history of hypertension of 7 years on average. Approximately 6% were diabetic with more than 10 years of diabetic history; 9% had antecedents of alcohol intake, and 38% were active smokers.

Information on all variables was not available for 100% of the donors. It was especially reduced in cases of hepatitis B surface antibody and hepatitis B core antibody, according to those variables that started being systematically recorded in 2000.

In relation to hemodynamic conditions, 60% received dopamine (average doses of 8.2 μg/kg/min), 17% received norepinephrine (0.9 μg/kg/min), 6% received dobutamine (average doses of 7.9 μg/kg/min), and 3% received epinephrine (8.7 μg/kg/min). Approximately 30% of the donors did not receive any vasoactive drug; 16% received a combination of two drugs, and 0.7% received a combination of drugs.

The ICU admission mean time was approximately 3 days (68 hr), but the median time was 1.5 days (38 hr). Thirteen percent of the donors presented with cardiac arrest (mean time of arrest was 17 min), and 40% presented with severe hypotensive episodes with an average duration of 85 min during the donor management.

Bacterial infection was diagnosed in 13% of the donors. Some of them (1%) were anti-HCV positive, 23% tested positive for hepatitis B core antibody, 33% tested positive for hepatitis B surface antibody, and 77% were positive for cytomegalovirus.

Biochemical data can be summarized as follows: mean liver enzyme values were 60.4 U/L for aspartate aminotransferase, 48.5 U/L for alanine aminotransferase, and 45.7 U/L for γ-glutamyltransferase. Total bilirubin average value was 1 mg/dL, with a mean direct bilirubin value of 0.4 mg/dL. Alkaline phosphatase was 134 U/L. Serum sodium mean value was 147.2 mEq/L, and serum potassium mean value was 3.7 mEq/L. Mean pH value was 7.4 with a bicarbonate average value of 22 mEq/L and PO_2 values of 130.7 mm Hg.

The mean prothrombin activity was 74.8%. Echography was performed in most donors, and there were signs of steatosis in 6% of them.

Bivariate Survival Analysis

Some donor variables showed statistical significance ($P<0.05$) in relation to liver graft survival: donor age, cause of death, body mass index, hypertensive antecedents, abnormal liver enzymes or alkaline phosphatase, time in the ICU, bicarbonate level, dopamine doses, and norepinephrine administration.

Graft survival was better when the donor age was less than 50 years (5-year survival rate of 68%) compared with grafts from donors aged between 50 and 69 years (5-year survival rate of 57%) and more than 70 years (5-year survival rate of 48%) ($P<0.05$). However, there are no statistically significant differences between the last two groups.

Graft survival was better when the cause of death was traumatic (5-year graft survival of 67%) compared with those in whom the cause of death was a stroke (5-year survival rate of 59%) ($P<0.05$). No significant differences were found for other donors' causes of death.

Grafts from donors with higher body mass index (>25) showed a lower survival rate at 5 years (60%) compared with those from donors with body mass index less than 25 (65%); however, differences were not statistically significant.

Graft survival was worse when the organ donor had hypertensive antecedents (history of hypertension >3 years and associated antihypertensive treatment) (Fig. 1). The same can be said when at least one of the three tested liver enzymes (aspartate aminotransferase, alanine aminotransferase, and γ-glutamyltransferase) was more than 200 U/L. These differences are more evident at short term (1-year graft survival of 78% and 72%, respectively) and minimal at medium term (5-year survival of 62% and 60%, respectively). Grafts from donors with higher alkaline phosphatase activity (>200 U/L) had worse survival at medium term (5-year survival of 53%) compared with grafts from donors with normal values (5-year survival of 62%). Time in the ICU had a significant influence on graft survival, which was better when the donor had been in the ICU for fewer than 6 days (Fig. 2). Bicarbonate level showed some impact on graft survival; higher differences were found between levels less than or more than 18 mEq/L (Fig. 3).

Dopamine infusion more than 15 μg/kg/min was associated with worse graft survival. On the other hand, norepinephrine administration was associated with better survival.

TABLE 1. Analysis of donor's characteristics

	N	Mean	SD	Proportion
Age (yr)	5,150	44.2	18.5	–
Weight (kg)	5,129	71.9	12.5	–
Height (cm)	4,988	168.4	9.5	–
Body mass index	4,988	25.3	3.8	–
Sex				
Male	3,252	–	–	63.1%
Female	1,898	–	–	36.9%
Blood group				
O	2,162	–	–	42%
A	2,373	–	–	46.1%
B	425	–	–	8.3%
AB	190	–	–	3.7%
Cause of death				
Stroke	2,775	–	–	53.9%
Trauma	1,967	–	–	38.2%
Other	408	–	–	7.9%
History of hypertension				
No	2,890	–	–	75.7%
Yes	926	–	–	24.3%
Length (yr)	172	6.7	6.7	
History of diabetes mellitus				
No	3,325	–	–	94.2%
Yes	204	–	–	5.8%
Length (yr)	48	10.4	9.0	
History of alcohol intake				
No	2,602	–	–	91.1%
Yes	253	–	–	8.9%
Cigarette smoking				
No	1,291	–	–	61.9%
Yes	796	–	–	38.1%
Dopamine infusion				
No	2,071	–	–	40.5%
Yes	3,043	–	–	59.5%
Dose (μg/kg/min)	3,013	8.2	5.3	
Norepinephrine infusion				
No	4,228	–	–	82.7%
Yes	882	–	–	17.3%
Dose (μg/kg/min)	849	0.9	3.3	
Dobutamine infusion				
No	4,796	–	–	93.9%
Yes	314	–	–	6.1%
Dose (μg/kg/min)	302	7.9	7.1	
Epinephrine infusion				
No	4,965	–		97.2%
Yes	145	–	–	2.8%
Dose (μg/kg/min)	123	0.7	1.5	
Cardiac arrest				
No	3,432	–	–	87.4%
Yes	493	–	–	12.6%
Time (min)	341	17.0	13.8	

TABLE 1. *Continued*

	N	Mean	SD	Proportion
Hypotension				
No	2,918	–	–	66.7%
Yes	1,456	–	–	33.3%
Time (min)	833	85.2	123.4	
Bacterial infection				
No	4,480	–	–	87%
Yes	670	–	–	13%
HCV Ab				
Negative	4,982	–	–	99%
Positive	63	–	–	1%
CMV Ab				
Negative	841	–	–	22.7%
Positive	2,857	–	–	77.3%
HBc Ab				
Negative	588	–	–	76.9%
Positive	177	–	–	23.1%
HBs Ab				
Negative	217	–	–	67%
Positive	107	–	–	33%
Abdominal echography				
Normal	2,139	–	–	93.7%
Altered	144	–	–	6.3%
AST (U/L)	3,743	60.4	105.0	–
ALT (U/L)	3,768	48.5	81.7	–
GGT (U/L)	2,665	45.7	79.3	–
Total bilirubin, serum (mg/dL)	3,419	1.0	2.3	–
Direct bilirubin, serum (mg/dL)	1,157	0.4	0.4	–
Alkaline phosphatase, serum (U/L)	3,676	134.0	100.6	–
Sodium, serum (mEq/L)	4,925	147.2	10.0	–
Potassium, serum (mEq/L)	3,973	3.7	0.7	–
pH, blood	3,691	7.40	0.1	–
Bicarbonate, arterial blood (mEq/L)	3,659	21.8	3.9	–
P_{AO_2}, arterial blood gases (mm Hg)	2,003	130.7	56.1	–
Hematocrit (%)	3,965	34.5	7.0	–
Platelet count (per microliter)	3,841	180,599	165,863	–
Protrombine activity (%)	3,302	74.8	19.2	–
Fibrinogen, plasma (mg/dL)	2,505	415.1	217.7	–
Glucose, plasma (mg/dL)	3,378	174.2	75.8	–
Serum protein level (g/dL)	2,484	5.5	1.1	–
Albumin, serum (g/dL)	380	3.1	1.0	–
Amylase, serum (U/L)	1,260	249.1	521.5	–
Lactate dehydrogenase, serum (U/L)	2,401	568.1	450.1	–
ICU admission (hr)	4,113	68.5	91.6	–

Number of donors with data recorded, mean and standard deviation for quantitative variables, and proportion for qualitative variables.
SD, standard deviation; HCV, hepatitis C virus; Ab, antibody; CMV, cytomegalovirus; ICU, intensive care unit; HBc Ab, hepatitis B core antibody; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-glutamyltransferase.

The norepinephrine dosage did not show any statistically significant differences when analyzed for three different levels: 0.5 μg/kg/min, 0.8 μg/kg/min, and 1 μg/kg/min. Graft survival was better when norepinephrine was administered alone than when dopamine was administered alone, when there was no vasoactive treatment, and when norepinephrine was associated with dopamine, although the differences were not statistically significant ($P<0.09$) (Fig. 4).

Diabetic antecedents (diabetes for >3 years and associated antidiabetic treatment) and the presence of prolonged

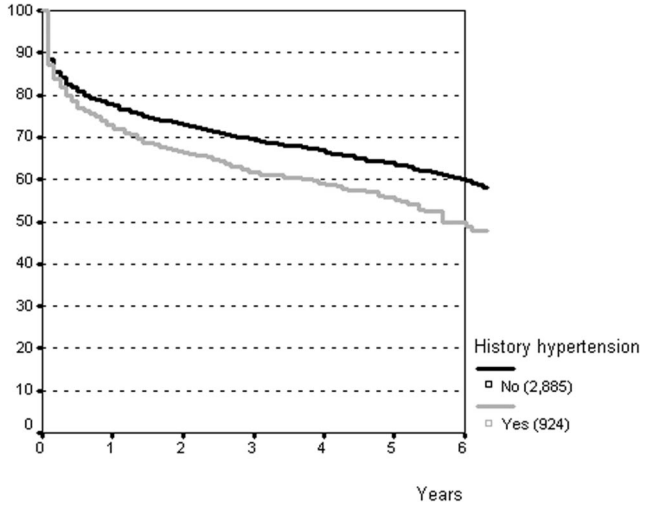

FIGURE 1. Liver graft survival in relation to the presence of donor hypertension antecedents ($P=0.0007$).

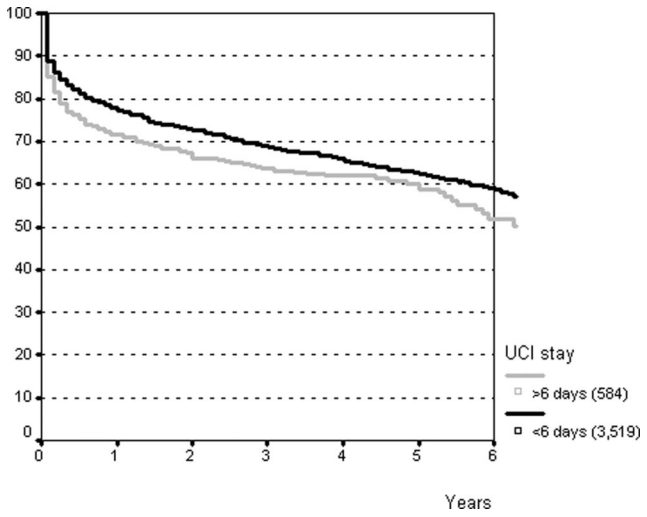

FIGURE 2. Liver graft survival in relation to intensive care unit (ICU) donor stay ($P=0.0011$).

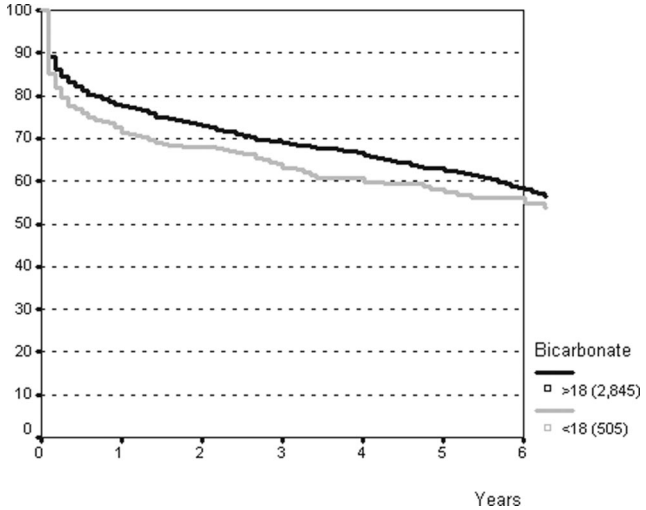

FIGURE 3. Liver graft survival in relation to donor serum bicarbonate level ($P=0.0052$).

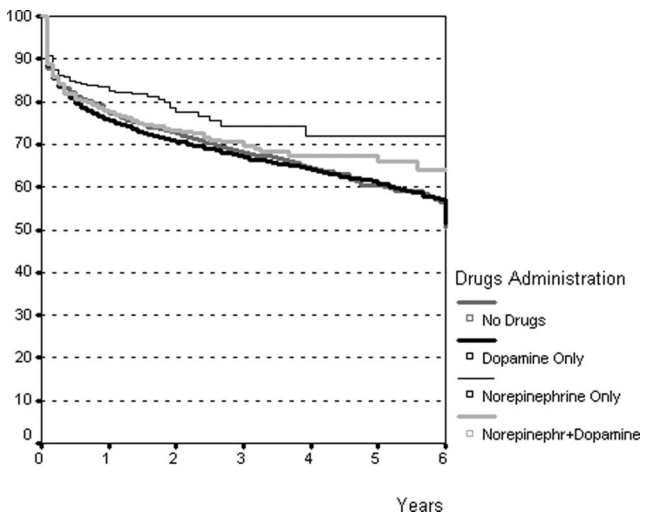

FIGURE 4. Liver graft survival in relation to drugs administration to the donor. (Norepinephrine only vs. dopamine only or no drugs: $P<0.05$. Rest of the comparisons: $P>0.05$.)

hypotension (>2 hr) during the donor management were statistically significant for a poor survival ($P=0.076$ and $P=0.71$ respectively).

The other analyzed variables did not show any impact on graft survival.

Multivariate Analysis

Information on the 27 variables were entered in the multivariate analysis for 3,429 grafts. The variables included were as follows: donor's age, cause of death, norepinephrine infusion, body mass index, liver enzymes, alkaline phosphatase, serum sodium, bicarbonate, history of hypertension, history of diabetes, duration of hypotension, ICU stay, and dopamine dose as donor's characteristics; severity, anti-HCV, ABO compatibility, recipient age, primary liver disease, and sex match as recipient's characteristics; and number of transplants, ischemic time, bypass, transplant period, average year activity, urgency, associated transplant, and perfusion liquid as technical characteristics.

Donor variables associated with graft survival ($P<0.05$) after the Cox proportional hazards method are shown in Table 2 and were as follows: age more than 50 years (RR=1.27), age more than 70 years (RR=1.4), hypertension ($P=0.05$) (RR=1.16), serum bicarbonate level less than 18 mEq/L (RR=1.27), ICU stay more than 6 days (RR=1.21), and norepinephrine administration during donor management (RR=0.79, protective effect)

Other donor variables that were significant, or almost significant, on the univariate analysis lost their statistical power when introduced on the Cox regression multivariate model: cause of death, body mass index, liver enzyme serum level, alkaline phosphatase, serum sodium, diabetes mellitus antecedents, hypotension, and dopamine administration.

TABLE 2. Proportional hazards (Cox) model for liver graft survival

Donor's characteristics	N°	RR (CI 95%)	*P*
Donor's age			
16–49 yr	1,879		
0–15 yr	105	1.03 (0.7–1.4)	0.00
50–69 yr	1,166	1.27 (1.1–1.4)	
≥70 yr	279	1.40 (1.1–1.8)	
Norepinephrine infusion			
No	2,668		0.01
Yes	761	0.79 (0.6–0.9)	
Bicarbonate			
>18 mEq/L	3,018		0.00
<18 mEq/L	411	1.27 (1.1–1.5)	
History of hypertension			
No	2,673		0.05
Yes	756	1.16 (1.01–1.3)	
ICU stay			
<6 d	2,939		0.03
>6 d	490	1.21 (1.1–1.4)	
Recipient's characteristics			
Severity			
At home	913		0.00
ICU	284	1.59 (1.1–2.4)	
Hospitalized	359	1.72 (1.3–2.1)	
Medical care	1,873	1.15 (0.9–1.3)	
Anti-HCV			
Negative	2,037		0.00
Positive	1,392	1.30 (1.1–1.5)	
Compatibility ABO			
Identical	3,258		0.00
Compatible	139	1.26 (0.9–1.6)	
Incompatible	32	2.23 (1.3–3.5)	
Primary liver disease			
Cholestatic disease	205		0.00
Cirrhosis	2,202	1.02 (0.7–1.4)	
Acute liver failure	152	1.19 (1.07–1.5)	
Malignancy	695	1.23 (1.0–1.6)	
Metabolic	85	1.45 (0.8–2.3)	
Others	90	1.83 (0.8–2.6)	
Technical characteristics			
Number of transplants			
1st	3,099		0.00
2nd, 3rd, 4th	330	1.51 (1.2–1.9)	
Average year activity			
≥de 50 transplants	1,564		0.00
<de 50 transplants	1,865	1.28 (1.1–1.5)	
Associated transplant			
No	3,370		0.00
Yes	59	1.86 (1.2–2.8)	

Spain (1994–2001). Variables with statistically significant impact on graft survival.
RR, relative risk; CI, confidence interval; ICU, intensive care unit.

Recipient and transplant factors associated with less graft survival ($P<0.05$) were as follows: second or third graft (RR=1.51), ABO compatibility instead of identity (RR=1.26), ABO incompatibility (RR=2.23), positive recipient HCV serology (RR=1.3), recipient on the ICU before transplant (RR=1.59), hospitalized recipient (RR=1.72),

acute liver failure (RR=1.19), recipient with hepatocellular carcinoma (RR=1.23), other associated solid-organ transplant (RR=1.86), and mean annual center activity of fewer than 50 liver transplants (RR=1.28)

Other recipient and technique variables were introduced in the regression model, but they did not reach the level of statistical significance: recipient age, sex compatibility between donor and recipient, ischemia time, type of bypass perfusion liquid, and urgency code.

The transplantation period was introduced in the analysis but remained within the limit of statistical significance (P=0.08).

DISCUSSION

This study presents the univariate analysis of the survival of 5,150 liver grafts performed in adult recipients between 1994 and 2001 in relation to 52 donor variables. Multivariate analysis was performed for 3,429 liver grafts through a Cox proportional hazard model including 26 variables from the donor, recipient, and graft technique.

Some of the results are consistent with published data, and other results are new. Donor age has been described as a risk factor for graft survival in different studies (*4–8*). This is, of course, found in our study; however, there are other analyzed variables showing the same or higher risk ratios. RR for losing the graft when the donor is aged more than 50 years is 1.27. The same RR can be found in the following cases: bicarbonate serum level of the donor less than 18 mEq/L; mean annual transplant center activity fewer than 50 transplants; and ABO compatibility between donor and recipient instead of identical matching. RR for grafts from donors aged more than 70 years (1.40) is less than the RR presented by retransplantation (RR=1.51) or the presence of an associated solid-organ transplantation (RR=1.86).

Elderly donors cannot simply be discarded as liver donors, but they must be carefully evaluated especially in relation to the development of atheromatosis (*20*). In such cases, it becomes mandatory to avoid other risks and be extremely attentive to the presence of hypertension (increased RR=1.16).

The prolonged donor ICU stay has been described by some authors as a risk factor (*3*, *14*); however, other studies did not find any impact (*8*, *16*, *21*). In our analysis, an ICU stay more than 6 days represents a moderate risk (RR=1.21). This can be explained by the associated parenteral nutrition, presence of infections, and a more aggressive hemodynamic donor management.

In regard to the hemodynamic donor management, some published data showed lower survival rates in cases of donors presenting acidosis (*14*). Nevertheless, we and others (*16*) did not find differences when pH values were analyzed. We found a worse graft survival when donor bicarbonate level was low (<18 mEq/L). This seems to be consistent with the presence of metabolic acidosis, because bicarbonate level varies more slowly than pH level when correction measures are applied.

The protective effect that norepinephrine administration showed on graft survival is the most novel result in our study. Encephalic death status presents an initial abdominal vasoconstriction followed by vasodilatation, generating a decrease in the perfusion pressure. After encephalic death is established, endogenous levels of norepinephrine decreased significantly below basal levels (*22*), leading to hypoperfusion, which can be overcome with exogenous norepinephrine administration. The protective effect that we found in our study is maintained even with doses more than 1 μg/kg/min, and the results are better when norepinephrine is administered alone without dopamine. In fact, dopamine treatment with doses greater than 15 μg/kg/min showed the opposite effect. It is not clear whether acidosis (which is frequent among organ donors) affects the efficacy of dopamine administration. Some studies found lower survival rates of the liver grafts when the donors were treated with high doses of vasoactive drugs (*3*). However, there are no consistent results in some of the published data. A higher proportion of primary nonfunction has been described for heart transplants when donors were treated with norepinephrine, but this was not the case for liver or renal grafts. In the case of renal transplants, the results were even better (*23*).

Perhaps the analysis of the effect of the vasoactive drug administration should take into account other factors such as average blood pressure, maximum and minimum administered doses, time of drug administration, venous filling pressure, and other hemodynamic management parameters.

Sodium level did not affect graft survival in our study. Survival rates at 1 and 3 months, and 1 and 5 years were similar when the serum sodium level in the donor was greater or less than 160 mEq/L. When a threshold was placed on 170 mEq/L, there were some differences, but they were not statistically significant because only 2% of the donors had sodium levels greater than 170 mEq/L. Some authors found that higher levels of serum sodium negatively affected graft survival or were related with a higher proportion of primary nonfunction in grafts (*8*). Nevertheless, this was not corroborated in other studies (*21*). These differences may be because the correction of the sodium level is crucial and only the sustained hypernatremia represents a risk factor for liver graft survival (*24*).

From our study one can conclude that there are several donor factors that negatively affect graft survival: elderly donors, antecedents of hypertension, prolonged ICU stay, and a decrease in the serum bicarbonate level. On the other hand, norepinephrine administration may represent a protective factor. These results appear when controlling donor variables with recipient variables and some technical aspects of the grafting process itself. In that way, among the 26 variables entered in the multivariate analysis, we identified some characteristics as risk factors that were also described by other authors: ICU or hospital recipient stay just before transplantation (*7*); positive HCV serologic status in the recipient (*5*); ABO compatibility between donor and recipient instead of identical matching (*16*); acute liver failure or hepatocellular carcinoma as primary cause for liver transplantation (*21*); second or third graft (*25*); associated solid-organ transplantation; and a low mean transplant annual activity in the transplant center (*26*).

There is some controversy in the identification of the factors that affect liver graft survival. These discrepancies may be attributable to the differences in the number of studied cases or the limited number of analyzed variables. Most of the studies are retrospective analyses and need to be adapted to

the available information, which seldom is 100% in all analyzed clinical charts. At the same time, it has to be emphasized that there was no previous definition of the data-collecting process. All of these factors impose limitations on the data analysis.

However, the high number of transplants analyzed in the present study allows us to establish some working hypothesis that needs further study. This includes the role of the norepinephrine administration or the presence of metabolic acidosis. We are currently conducting a prospective multicenter study (in which most Spanish liver transplant centers are involved) that will be completed in 2006 and that will better identify the risk factors for liver graft survival.

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REFERENCES

1. Council of Europe. International figures on organ donation and transplantation in 2003. *Transplant Newsletter* 2004; 9(1): 18–20.
2. Miranda B, Vilardell J, Grinyo JM. Optimizing cadaveric organ procurement: the Catalan and Spanish experience. *Am J Transplant* 2003; 3(10): 1189–1196.
3. Briceno J, Marchal T, Padillo J, et al. Influence of marginal donors on liver preservation injury. *Transplantation* 2002; 74(4): 522–526.
4. Detre KM, Lombardero M, Belle S, et al. Influence of donor age on graft survival after liver transplantation—United Network for Organ Sharing Registry. *Liver Transpl Surg* 1995; 1(5): 311–319.
5. Velidedeoglu E, Mange KC, Frank A, et al. Factors differentially correlated with the outcome of liver transplantation in HVC+ and HCV- recipients. *Transplantation* 2004; 77(12): 1834–1842.
6. Busquets J, Xiol X, Figueras J, et al. The impact of donor age on liver transplantation: influence of donor age on early liver function and on subsequent patient and graft survival. *Transplantation* 2001; 71(12): 1765–1771.
7. Smith CM, Davies DB, McBride MA. Liver transplantation in the United States: a report from the Organ Procurement and Transplantation Network. In: JM Cecka, Terasaki PL, eds. Clinical transplants, 2000. UCLA Tissue Typing Laboratory. Los Angeles, CA: 2001, pp 19–30.
8. Markmann JF, Markmann JW, Markmann DA, et al. Preoperative factors associated with outcome and their impact on resource use in 1148 consecutive primary liver transplants. *Transplantation* 2001; 72(6): 1113–1122.
9. Russo MW, Galanko JA, Zacks SL, et al. Impact of donor age and year of transplant on graft survival in liver transplant recipients with chronic hepatitis C. *Am J Transplant* 2004; 4(7): 1133–1138.
10. Berenguer M, Prieto M, San Juan F, et al. Contribution of donor age to the recent decrease in patient survival among HCV-infected liver transplant recipients. *Hepatology* 2002; 36(1): 202–210.
11. Marino IR, Doyle HR, Aldrighetti L, et al. Effect of donor age and sex on the outcome of liver transplantation. *Hepatology* 1995; 22(6): 1754–1762.
12. Brooks BK, Levy MF, Jennings LW, et al. Influence of donor and recipient gender on the outcome of liver transplantation. *Transplantation* 1996; 62(12): 1784–1787.
13. Mor E, Klintmalm GB, Gonwa TA, et al. The use of marginal donors for liver transplantation. A retrospective study of 365 liver donors. *Transplantation* 1992; 53(2): 383–386.
14. Deschenes M, Belle SH, Krom RA, et al. Early allograft dysfunction after liver transplantation: a definition and predictors of outcome. National Institute of Diabetes and Digestive and Kidney Diseases Liver Transplantation Database. *Transplantation* 1998; 66(3): 302–310.
15. Castellvi JM, Xiol X, Guardiola J, et al. Pretransplantation risk factors for graft loss after liver transplantation in cirrhotic patients; effect of cytomegalovirus serologic status. *Transpl Int* 2004; 17(3): 131–137.
16. Hoofnagle JH, Lombardero M, Zetterman RK, et al. Donor age and outcome of liver transplantation. *Hepatology* 1996; 24(1): 89–96.
17. Koneru B, Dikdan G. Hepatic steatosis and liver transplantation current clinical and experimental perspectives. *Transplantation* 2002; 73(3): 325–330.
18. Ureña MA, Ruiz-Delgado FC, Gonzalez EM, et al. Assessing risk of the use of livers with macro and microsteatosis in a liver transplant program. *Transplant Proc* 1998; 30: 3288–3291.
19. Ont.es [homepage on the internet]. Madrid: Organización Nacional de Trasplantes. [Updated 2004 May 1; cited 2004 Sep 9]. Available at: http://www.ont.es/esp/estadisticas/f_estadisticas.htm. Accessed April 6, 2005.
20. Grazi GL, Cescon M, Ravaioli M, et al. A revised consideration on the use of very aged donors for liver transplantation. *Am J Transplant* 2001; 1(1): 61–68.
21. Ghobrial RM, Steadman R, Gornbein J, et al. A 10-year experience of liver transplantation for hepatitis C: analysis of factors determining outcome in over 500 patients. *Ann Surg* 2001; 234(3): 384–393.
22. Herijgers P, Leunens V, Tjandra-Maga TB, et al. Changes in organ perfusion after brain death in the rat and its relation to circulating catecholamines. *Transplantation* 1996; 62(3): 330–335.
23. Schnuelle P, Berger S, de Boer J, et al. Effects of catecholamine application to brain-dead donors on graft survival in solid organ transplantation. *Transplantation* 2001; 72(3): 455–463.
24. Totsuka E, Dodson F, Urakami A, et al. Influence of high donor serum sodium levels on early postoperative graft function in human liver transplantation: effect of correction of donor hypernatremia. *Liver Transpl Surg* 1999; 5(5): 421–428.
25. Ghobrial RM, Gornbein J, Steadman R, et al. Pretransplant model to predict posttransplant survival in liver transplant patients. *Ann Surg* 2002; 236(3): 315–322.
26. Edwards EB, Roberts JP, McBride MA, et al. The effect of the volume of procedures at transplantation centers on mortality after liver transplantation. *N Engl J Med* 1999; 341(27): 2049–2053.