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Does the Presence of a Measurable Blood Alcohol Level in a Potential Organ Donor Affect the Outcome of Liver Transplantation?

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The widespread application of hepatic transplantation has created a tremendous demand for donor organs. An assessment of donor parameters is thought to be important in selecting good donors; however, the criteria utilized have not been standardized. This study was performed to determine the effect of a measurable donor blood alcohol level on graft survival. Fifty-two patients who underwent orthotopic liver transplantation at the University of Pittsburgh were included in the study. Twenty-five patients received liver grafts from donors having a blood alcohol level between 0.04 and 0.4 g/l with a mean of 0.17 g/l. Twenty-seven patients received a liver graft from a donor who had no measurable blood alcohol. There were no differences between these two groups of donors regarding the time of initial hospitalization until the time of donation. Graft failure within the first 30 days was 24% for those receiving an organ from an alcohol-positive donor as compared with 22.2% in those receiving an organ from an alcohol negative donor. The recipient mortality rate was 16% and 11%, respectively. No relationships between the donor blood alcohol level and organ performance, frequency of primary graft nonfunction, or number of episodes of acute cellular rejection were evident. Based upon these data, the presence of a measurable blood alcohol level in a donor should not mitigate against organ donation.

Key Words: Alcoholic Intoxication, Graft Survival, Donor's Criteria, OLTx, Organ Donation.

HEPATIC TRANSPLANTATION is the ultimate therapeutic option in the clinical management of many hepatic diseases.[1,2] It currently is available at many centers worldwide and its widespread application has created a tremendous demand for donor organs. A paucity of donor organs has always been an important problem limiting the full application of liver transplantation.[3] As the indications for liver transplantation have been expanded and the number of individuals with liver disease waiting to be transplanted has expanded, the paucity of donor organs has become even more problematic.[1] One approach to this problem has been the utilization of donors that previously were rejected because of their age, vascular instability, and confounding medical illnesses such as diabetes and alcohol abuse.[4]

Despite such changes in the acceptability of potential donors, the continuous expansion of the pool of recipients has not been matched by an equivalent expansion of the pool of available donor organs. This discrepancy between the number of acceptable donors and recipients has lead to and continues to result in recipients dying while waiting to be transplanted. On the other hand, transplantation of unsound organs can lead to the unnecessary death of recipients or an accelerated need for retransplantation.[3] As a result, attempts to assess the quality of potential liver donors has become an important function of organ procurement organizations and transplant surgeons.[5] However, the criteria utilized by different centers have not been standardized nor have previous attempts to correlate donor characteristics with subsequent transplantation outcome been particularly successful.[6] Even if an accurate assessment of donor hepatic function were possible prior to organ procurement, the subsequent events (e.g., preservation and reperfusion injury) may be over-riding issues limiting donor organ function following engraftment.[7]

Many donors die as a result of motor vehicle accidents, intracranial hemorrhage, head injury, aspiration and drug intoxication.[5] Ethanol intoxication is encountered frequently in many of these same situations. Recently, it has been shown that donor livers with histologic macrovesicular steatosis function less well than do those with microvesicular steatosis and as a result use of these grafts is associated with a greater frequency of subsequent graft nonfunction.[8] Alcohol abuse is a common cause of hepatic macrovesicular steatosis.[9] The following study was initiated therefore to determine the effect of an elevated donor blood alcohol level obtained at the time of hospitalization of the donor on hepatic graft survival following liver transplantation.

MATERIALS AND METHODS

Study Population

One hundred fifty consecutive donors' records from the University of Pittsburgh's organ procurement office were reviewed retrospectively beginning on March 1989 and continuing through December 31, 1989. Only 44.7% ($n = 67$) had their blood alcohol level determined, and thus the remaining donors could not be included in the study. Thirty-four donors with a detectable blood alcohol level at the time of hospitalization were identified and served as the study group. Six of these were excluded from subsequent study as their organs were transplanted into recipients undergoing retransplantation. Three additional donors were eliminated

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from study because they were utilized as part of a multivisceral transplantation procedure.

The second group consisted of thirty-three donors who had undetectable blood alcohol levels at the time of their initial hospitalization; thus they constituted the control group. Six of these donors were excluded from subsequent study because their organs were utilized by recipients undergoing retransplantation procedures in five cases, and the organ of the sixth was used as part of a multivisceral transplantation procedure.

The donor variables that were assessed for each group as factors possibly relevant to subsequent successful graft function were the donors' age, gender, reason for hospitalization, time interval from hospitalization to actual donation, blood ethanol level, serum aspartate transaminase (SGOT), serum alanine transaminase (SGPT), total bilirubin level, and the prothrombin time.

The recipients' records were reviewed as well with particular attention being given to the age, sex, primary liver disease, back table biopsy findings, postrevascularization liver biopsy findings, initial graft function, graft survival, and recipients survival within the first 30 days following transplantation.

Definitions

Primary graft nonfunction (PGN) was defined as irreversible failure of the graft to function occurring within 7 days of transplantation for which no other cause could be identified.

Acute cellular rejection was defined as a mononuclear portal tract inflammation with evidence of bile duct damage with or without subendothelial inflammation.[10]

Chronic rejection was defined as loss of small bile ducts and arteries or arterial mural thickening and hyalinization.[10]

Ischemic changes were defined as the presence of fine microvesicular steatosis with an accumulation of neutrophils in the sinusoids near cellular debris associated with central hepatocanalicular cholestasis.[8]

Statistical Analysis

Results are reported as mean values ±SEM. Associations and differences in proportions were analyzed using Chi square test. Fisher's exact test was used as required; 2-way analysis of variance was used to test differences in mean values of the continuous variables. The estimated survivals were calculated and compared using generalized savage (Mantel-Cox) and Wilcoxon (Brenslow) Life Table analysis using the BMDP-2L statistical software package (University of California). A p value of <0.05 was considered to be statistically significant.

RESULTS

Of the 25 recipients receiving an organ from a donor known to have a measurable blood level alcohol at time of initial hospitalization, 12 were males and 13 were female and their mean age was 44.1 ± 2.6 years. The 25 donors consisted of 19 males and six females with a mean age of 26.4 ± 1.3 years. Fourteen of the 25 recipients received a donor organ that was gender matched, while nine female recipients received grafts from male donors and two males received their grafts from female donors.

These donors could be divided into three groups based upon the level of blood ethanol at the time of initial hospitalization:

Group 1 (n = 8), serum ethanol level <0.1 g/l (x = 0.07 ± 0.01)
Group 2 (n = 4), serum ethanol level 0.11–0.19 g/l (x = 0.14 ± 0.01)
Group 3 (n = 13), serum ethanol level >0.2 g/l (x = 0.24 ± 0.01)

Twenty-seven recipients received organs from donors without measurable blood alcohol levels at the time of initial hospitalization. Nineteen of the recipients were male and eight were female with a mean age of 49.9 ± 2.5 years. The 27 donors consisted of 15 males and 12 females with a mean age of 30.9 ± 2.4 years. Gender matching between the donor and the recipient occurred in 21 cases, while in six there was a mismatch with five males receiving a graft from a female donor and only one female who received a male liver graft.

The donor characteristics of the two groups are shown in Table 1. The characteristics of each group are segregated into those present in donors whose organs ultimately failed and those that functioned following surgical engraftment. No statistical differences were noted between the various groups. Table 2 shows the graft outcome for both donor groups further segregated as to the cause of graft injury following surgical engraftment. Again, no differences among graft outcome categories in the two groups were evident. Table 3 shows the data for graft outcome of those organs obtained from donors with a measurable blood alcohol level divided into categories based upon the blood alcohol level in the donor at the time of initial hospitalization. No statistical differences were evident for any specific cause of graft failure or for graft survival (Figs. 1B and 2B) as a function of the blood alcohol level.

Table 4 segregates failed grafts in the alcohol positive

Table 1. Characteristics of the Two Donor Groups

Group	Graft outcome	Number (n)	Age (yrs)	Time until donation (days)	SGOT (IU/l)	SGPT (IU/l)	Total bilirubin (mg/dl)	Prothrombin time (seconds)
Alcohol-positive	Graft failure	6*	23 ± 1.7	2.6 ± 0.7	79 ± 22.6	33 ± 8	0.7 ± 0.2	14 ± 0.7
n = 25	No failure	19	28 ± 1.5	2.6 ± 0.4	93 ± 16.9	48 ± 13	0.6 ± 0.1	14 ± 0.3
Alcohol-free	Graft failure	5†	31 ± 2.4	5.6 ± 1.4	61 ± 18	33 ± 6	0.8 ± 0.1	13 ± 0.5
n = 27	No failure	22	31 ± 2.9	4.0 ± 0.7	47 ± 7.6	39 ± 9	0.7 ± 0.1	13 ± 0.3
Normal values					0–32	0–32	<1.0	12.0

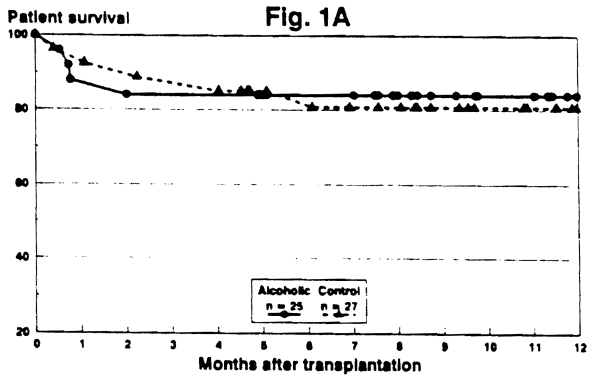
* 4 Primary graft nonfunction
2 Humoral rejection
† 2 Primary graft nonfunction
2 Humoral rejection
1 Hepatic artery thrombosis

Table 2. Graft Outcome in the Two Groups Studied

	Primary graft nonfunction	Humoral rejection	Cellular rejection	Ischemia	No dysfunction
Alcohol-positive $n = 25$	16% (4/25)	8% (2/25)	44% (11/25)	4% (1/25)	28% (7/25)
Alcohol-free n 27	7.4% (2/27)	0%	48.1 (13/27)	7.4 (2/27)	37.3% (10/27)

Table 3. Graft Outcome for Those Receiving a Graft from a Donor with a Measurable Blood Alcohol Level Segregated as to the Level of Blood Alcohol

Blood alcohol level	Primary graft nonfunction	Humoral rejection	Cellular rejection	Ischemia	No dysfunction
<0.1 g/l $n = 8$	12.5% (1/8)	0%	62.5% (5/8)	0%	25% (2/8)
0.10–0.19 g/l $n = 4$	0%	25% (1/4)	50% (2/4)	0%	25% (1/4)
>0.2 g/l $n = 13$	23.1% (3/13)	7.7% (1/13)	30.7% (4/13)	7.7% (1/13)	30.7% (4/13)



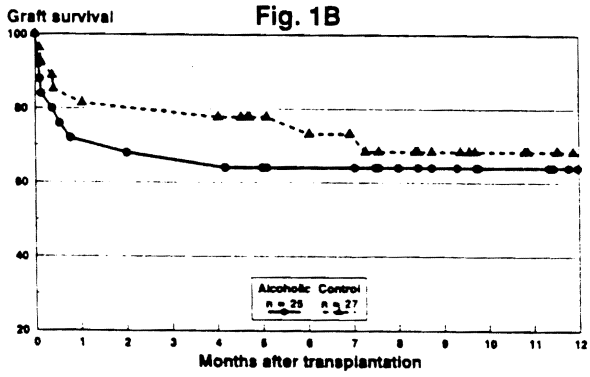
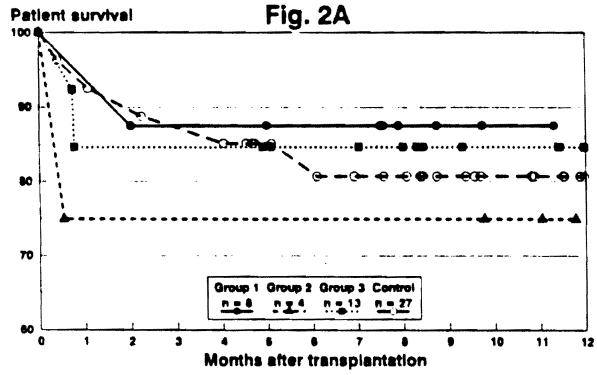


Fig. 1. Kaplan Meyer survival curves for recipients (A) and grafts (B) of the two donor groups studied

and alcohol free groups into groups based upon the timing of graft failure following transplantation. Again no difference between groups was evident. The ultimate recipient outcome for the alcohol free and alcohol positive groups experiencing primary nonfunction was 0% and 25% mortality rate, respectively. A higher death rate was noted in those receiving an organ from an alcohol positive donor, but because of the small number, this difference was not significant. The recipient mortality as a function of having received a donor organ from an alcohol free or alcohol positive donor was 16% vs 11%; no statistical difference between these groups was demonstrable (Fig. 1A). Finally recipient survival for those receiving an organ from an alcohol positive donor segregated as to the amount of



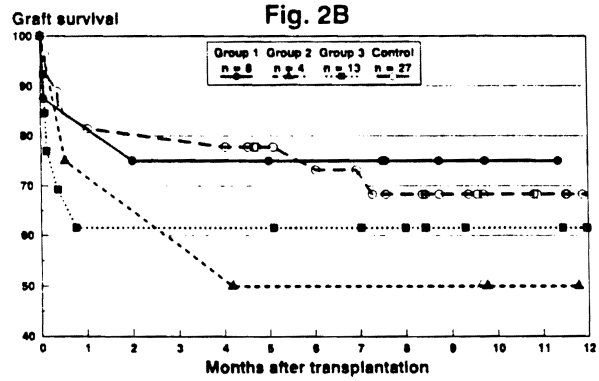


Fig. 2. Kaplan Meyer survival curves for recipients (A) and grafts (B) of the two donor group studied.

Table 4. Timing of Graft Failure within the First 30 Days Following OLTx

	1–15 Days	16–30 Days	Total
Alcohol-positive $n = 25$	20% (5/25)	4% (1/25)	24% (6/25)
Alcohol-free $n = 27$	14.8% (4/27)	3.7% (2/27)	22.2% (6/27)

Table 5. Recipient Mortality among Individuals Receiving an Alcohol Positive Donor Segregated as to Level of Blood Alcohol

	$n = 8$ <0.1	$n = 4$ 0.11–0.19	$n = 13$ >0.2
Expired	12.5%	25%	15.4%
Alive	87.5%	75%	84.6%

Table 6. Back Table and Postanastomosis Graft Biopsy

	Alcohol group ($n = 25$)		Control group ($n = 27$)	
Histopathology	Back table	Postanastomosis	Back table	Postanastomosis
Normal biopsy	5	3	10	11
Steatosis				
Micro	6	4	6	3
Macro	3	2	7	3
Mixed	5	3	2	1
Ischemia				
Mild	4	6	2	2
Moderate	2	4		4
Severe		3		2
	25	25	27	27

alcohol found in the donor is shown in Table 5 and Fig. 2A. Again, no statistical differences was evident. Histologic findings for backtable and post-revascularization graft biopsies are summarized in Table 6 and presented as

group finding as follows:

Alcohol-Positive Group

In eight of the alcohol-positive organs, some histological deterioration of the graft biopsy following reperfusion was noted. Five of these grafts ultimately failed: four due to primary graft nonfunction and one due to acute humoral rejection. In contrast, among the 17 alcohol-positive donor organs in which no apparent change in the liver appearance occurred following reperfusion, no graft failures were seen (Table 6).

Alcohol-free Group

In seven, some deterioration in the histologic appearance of the graft was demonstrable following reperfusion; two of these seven grafts failed as a result of primary graft nonfunction.

DISCUSSION

This study demonstrates that recipients of organs obtained from alcohol positive donors do equally following OLTx as do those obtained from donors who are alcohol-free. Further, higher donor blood alcohol levels are not associated with a poorer outcome in terms of graft dysfunction of any type, the frequency of primary graft failure, ultimate graft survival or recipient survival. Receiving a graft from a donor of a different gender had no effect on the outcome of the transplant.

Typically, donors of organs utilized for transplantation are individuals who are young, die suddenly and unexpectedly, usually as a result of an accident or injury.[5] Alcohol use is common in individuals who possess these particular characteristics. Thus, alcohol users/abusers as a group are over represented among organ donors.

Alcoholism is a common problem. In the United States alone, it is estimated that there are 9 million or more alcohol abusers.[10] Moreover, alcoholic liver disease is the 9th leading cause of death in the United States and occurs predominantly in those in their 3rd through 5th decades of life, typically the most productive years of an individual's life.[11,12] This time period also coincides with the ages at which most donors are recruited.

Despite their numbers, individuals with advanced alcoholic liver disease have been considered only recently as possible candidates for OLTx. Thus, taken as a group, alcohol abusers have been and continue to be underrepresented as recipients of liver transplants while at the same time being over represented in the donor population.[4]

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