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The prognostic significance of serum aspartate transaminase and gamma-glutamyl transferase in liver deceased donors

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ABSTRACT

The impact of aspartate transaminases (AST) and gamma-glutamyl transferase (GGT) in serum of deceased donors on outcomes after liver transplantation (LT) is unclear. This study aimed to explore the relationship between donor highest AST value or first donor GGT value and graft survival. All consecutive patients who underwent a primary LT in a single center with available donor AST (N = 1253) and GGT value (N = 1152) were included. There was no significant association between donor AST and 90-day graft survival. We found a moderate association between GGT and 90-day graft survival. We found a significant interaction with a donor history of alcohol abuse (HAA). The risk of graft loss was associated with AST and GGT in donors with an HAA but remains unchanged in donors without HAA. There was no difference in graft survival according to donor AST or GGT with a cutoff ≥95th percentile (475 UI/l for AST and 170 UI/l for GGT). However, graft survival was significantly decreased when donors combined GGT ≥ 170 UI/l and HAA (61% at one year). Hepatic grafts from donors with high AST or high GGT but without alcohol history and no additional risk factors can be transplanted in low-risk recipient.

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Key words
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Introduction

In liver transplantation (LT), accepting a graft remains a complex decision, involving several donor and recipient-related factors. Among them, donor liver function tests are part of the decision-making process. Biological abnormalities may suggest an underlying disease or severe liver injury, leading to decline the offer.

Donors with elevated bilirubin are excluded in the majority of cases [1], but abnormal transaminases or gamma-glutamyl transferase (GGT) in donor serum level do not contraindicate liver donation. However, experts of a consensus meeting on expanded donor criteria did not agree about an upper limit of transaminases, but propose the utmost caution for donors with GGT over 200 UI/l [2]. In fact, there is little evidence

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to support this statement, and references for interpreting the prognostic value of donor GGT or transaminases are lacking.

This study was undertaken to assess the prognostic significance of transaminases and GGT levels measured in the donor serum and to understand their relationship with the other donor factors. Our secondary aim was to report the outcomes of patients who were given grafts from donors with high AST or GGT.

Methods

Study population

We included all adult patients who underwent first orthotopic liver transplantation, with deceased brain donors, from the 1st January 2004 to 31st December 2018, at Paul Brousse hospital, Villejuif, France. Other donation circumstances like living donation, donation after cardiac death, or domino were excluded from the analysis. The design of this study was discussed and approved during our weekly research meeting. This study was achieved in accordance with ethical standards laid down in the 2000 Declaration of Helsinki as well as the Declaration of Istanbul 2008. All patients alive at the time of the analysis have given their informed consent for the retrospective analysis of data collected in the setting of routine health cares.

Donor evaluation

At the time of a graft offer, most essential variables of the donor are collected in C*ristal*, a dedicated database run by the *Agence of Biomédecine*, the national organization in charge of organ allocation in France. Data are fulfilled by local teams in charge of a potential donor and encompass a wide range of information related to the medical history of the donor, morphological parameters, biological tests, and evolution since admission and results from CT scan. After the approval of our research project by the *Agence of Biomédecine*, we obtained a complete export of our donor data.

Graft selection policy

We deliberately accepted marginal grafts, provided that they could be given to low-risk recipients, that is, those with long-expected waiting time and low risk of early spontaneous mortality. Grafts from donors with hyperbilirubinemia or liver dysmorphia on imaging were denied. In contrast, elderly donors or obese donors or donors with a history of alcohol abuse (HAA) were usually accepted as long as they did not cumulate additional adverse factors.

High serum level of transaminases did not preclude donation provided that the last value was inferior to the highest. The GGT serum level at the donor's admission was given the importance, but no clear cutoff limit was used to contraindicate transplantation. In the case of high first value, the decision was made on a case-by-case basis, according to the existence of additional donor risk factors and the senior surgeon appreciation.

Graft retrieval and transplantation

When the macroscopic aspect of the graft was suggestive of moderate or severe steatosis or fibrosis, liver biopsy with frozen section examination was routinely performed. In doubtful cases, pictures of the graft could be sent to the senior transplant surgeon. When graft was considered suitable, the recipient was transferred to the operating room, and operation was started without waiting for the graft return in order to reduce cold ischemia time as much as possible. We used the preservation liquid available at the donor hospital. Our transplantation technique was to preserve the caval flow during total hepatectomy every time it was deemed feasible [3, 4]. Porto-caval anastomosis was done routinely since 2013. Implantation was done according to the standard manner. Surgical liver biopsy at the end of transplantation is routinely performed.

Statistical analysis

Donor data were extracted from the *Cristal* database and merged with our prospectively maintained local database using the national donor number. We selected aspartate aminotransferase (AST), as a biomarker of liver injury [5, 6] to study the influence of donor transaminases. Donors without available measurement of GGT or AST were excluded. Missing variables were not treated by imputations and the analysis was done with available data. We focused on the maximal AST value and the first GGT value for the analysis because these values were used to decide to accept or reject graft at the time of the offer.

Prognostic assessment

Early allograft dysfunction (EAD) was defined, according to Olthoff *et al* [7]. One-year graft survival was calculated by using the time from LT to death or retransplantation at one year. Patients for whom an

Transplant International 2021; 34: 2247–2256

event of interest (death or retransplantation) occurred beyond one year were censored.

The risk for EAD and 90-day graft survival was calculated by using a logistic regression model, whereas a Cox proportional hazards model was used for one-year graft survival. The assumption of the proportional hazards was checked by using the method described by Grambsch and Therneau [8].

Donor AST and GGT were analyzed as continuous variables. Categorization, according to prespecified cut-off points, was avoided because of the several limitations inherent to this method [9, 10]. Both variables were transformed by using restricted cubic splines (with 3 knots) to relax from linearity assumption for continuous predictors [11, 12].

We included clinically meaningful covariates [13] to adjust for potentially confounding effects (Donor age, recipient age, MELD score, life support therapy at the time of urgent transplantation, and cold ischemia). The risk as a function of donor AST and GGT was plotted to enable a better understanding of their effect on outcomes of interest.

We finally tested for interaction between donor AST and GGT and other donor-related covariates, which allows evaluating how one donor covariate may affect the prognostic value of donor AST and GGT.

Grafts from donors with high maximal AST and first value GGT

Continuous variables and categorical variables were expressed a median (range) and percentage, respectively. Comparisons were made by using Chi-square test, or Fisher test or Wilcoxon test, as appropriate. High values were arbitrary, defined as any values equal to or higher than the 95th percentile. Survival probabilities were calculated with the Kaplan–Meier method and compared with the log-rank test. Statistical significance was defined by a P value <0.05. This analysis was made with R, using mainly *CompareGroups*, *survival*, and *ggplot2* packages.

Results

Description of the study population

Of the 1438 patients who underwent primary deceased brain donors LT over the study period, measurements of donor AST and GGT were available in 1253 and 1152 patients, respectively. Abnormal values of donor AST (>40 UI/l) or GGT (>50 UI/l) were observed in 65% and 46.5% of cases, respectively. The median (range) of donor AST (maximal value) and donor GGT (first value) were 58 UI/l (6-2000) and 30 UI/l (2-1147), respectively. Of note, grafts from donors with maximal AST ≥1000 UI/l or first GGT ≥500 UI/l were given to 25 (2.0%) and seven patients (0.6%), respectively.

Impact on early graft dysfunction, 90-day graft survival, and 1-year graft survival

We found that the Cox model's proportional-hazards assumption for overall graft survival could not be satisfied, indicating that donor AST and GGT yield a time-varying effect on outcomes. We observed that the effect of donor AST and GGT, when existing, was maximal during the first year and could be neglected in patients alive retransplant-free after one year (data not shown).

Maximal AST value

The risk for EAD, 90-day, and one-year graft survival as a function of donor AST is shown in Fig. 1. The risk increased from the lowest value to reach a maximal around 200 UI/l for the three end-points and tend to decrease after. The highest risk was observed for 90-day graft survival with an adjusted hazard ratio (HR) of 1.5. However, the lower limit of the confidence interval remained below 1. A significant association was therefore rejected.

First GGT value

Relative risk and hazard ratio, according to donor GGT, are given in Fig. 2. The adjusted risk for EAD and 90-day graft survival increased sharply from the lowest value to a value of about 100 UI/l and stabilized beyond. At this point, the lower limit of the confidence interval was higher than one, thus indicating significant association. There was no significant association between first GGT and one-year graft survival.

The prognostic value of first, last AST value and maximal, last GGT value

In addition, we tested the prognostic value of AST and GGT measured in other timings. Data are provided in a Fig. S1 for information purposes.

Evaluation of Interaction with other donor covariates

P values of interaction tests between donor covariates and donor AST or GGT are given in Table 1. We found

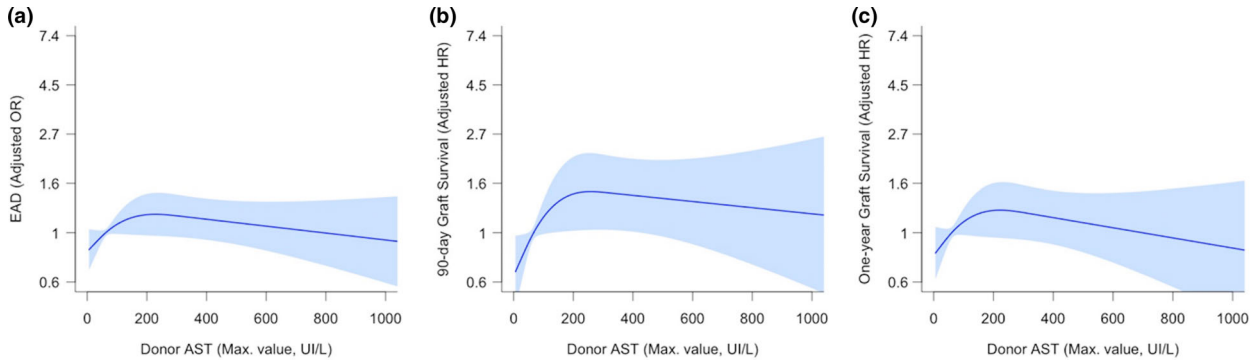

Figure 1 Impact of Donor AST (Maximal value) on early allograft dysfunction (a), 90-day graft survival (b), and one-year graft survival (c). Shaded regions indicate 95% confidence bands. EAD, early allograft dysfunction; HR, Hazard Ratio. OR, Odd ratio.

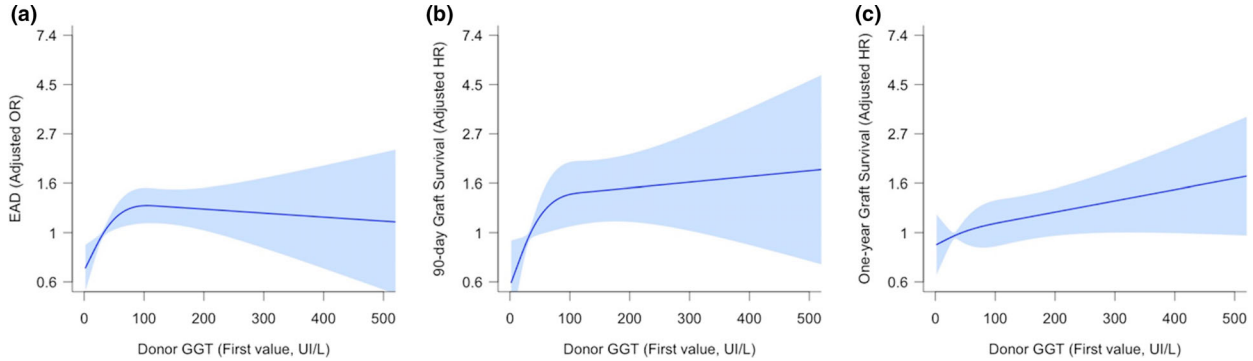

Figure 2 Impact of Donor GGT (First value) on early allograft dysfunction (a), 90-day graft survival (b), and one-year graft survival (c). Shaded regions indicate 95% confidence bands. EAD, early allograft dysfunction HR, Hazard Ratio. OR, Odd ratio.

Table 1. *P* values of interaction terms between donor-related variables.

	Donor AST (Maximum value)		
Donor Variables	EAD	90-day graft survival	1-year graft survival
Age	0.233	0.702	0.608
Obesity	0.169	0.062	0.037
Diabetes	0.911	0.539	0.245
HAA	0.205	0.042	0.037
Cardiac arrest	0.651	0.643	0.227
	Donor GGT (First value)		
	EAD	90-day graft survival	1-year graft survival
Age	0.098	0.462	0.144
Obesity	0.781	0.865	0.403
Diabetes	0.196	0.725	0.695
HAA	0.004	0.012	0.001
Cardiac arrest	0.795	0.428	0.817

P value of interaction term between donor variables and AST and GGT donor Y ~ X1+X2+...+Xn+X1:Vint*

*X1:Vint: Interaction term; Y, Outcomes; X1, donor AST or donor GGT; X2, Xn covariates for adjustment; Vint, variable of interest; EAD, early allograft dysfunction (Olthoff).

Transplant International 2021; 34: 2247–2256

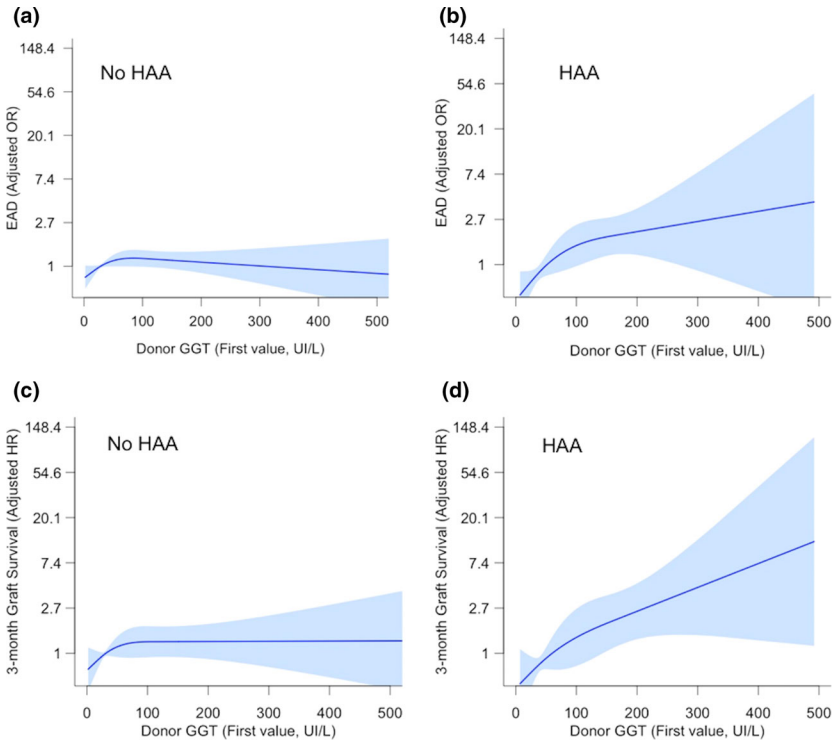

Figure 3 Risk for early allograft dysfunction and 3-month graft survival according to donor history of alcohol abuse. Shaded regions indicate 95% confidence bands. EAD, early allograft dysfunction; HAA, History of alcohol abuse; HR, Hazard Ratio. OR, Odd ratio.

a significant interaction between donor HAA and donor AST for 90-day and one-year graft survival. Similar findings were observed with donor GGT. Other covariates such as diabetes, obesity, cardiac arrest, and donor age did not influence the relationship between donor GGT and the risk of graft loss at one year.

To better understand the significance of this interaction, we plotted the risk for one-year graft survival according to donor drinking history (Fig. 3). Three-month graft survival remains little or unaffected by the increase of donor AST or GGT when there was no HAA (Fig. 3a and c). In contrast, the risk of graft loss at 3 months was much higher in donors with either high AST or high GGT and a history of alcohol abuse (Fig. 3b and d).

Grafts from donors with high AST or GGT value (≥95th percentile)

The 95th percentiles were 475 UI/l for AST and 170 UI/l for GGT.

Donors with maximal AST value

The comparison between donor and recipient characteristics according to 95th percentile of the maximal AST value is given in Table 2. Briefly, donors with AST ≥475 UI/l were younger and died from anoxia. Cardiac arrest before donation occurred more often, and its duration was longer. Rates of early death or retransplantation were similar, as well as graft survival. (Fig. 4a).

Donors with first GGT value

The characteristics and outcomes, according to GGT, are shown in Table 3. Briefly, donors with first GGT value ≥170 UI had increased body weight, body mass index, and liver weight. A HAA was also found more frequently, and the length of stay in intensive care was also longer in these donors. Grafts from donors with first GGT ≥170 UI/l were associated with a higher risk of retransplantation or death at 90 days.

Kaplan–Meier survival curves are presented in Fig. 4b. Although there was no statistically significant difference in graft survival, survival probabilities of grafts from a donor with high GGT tend to be lower at the early post-transplant period.

History of alcohol abuse in donors with high GGT

Among donors with high GGT, we compared outcomes and histology (from end-LT liver biopsy) according to donor HAA (Table 4). One-year graft survival was

Table 2. Comparisons of recipient, donor, and outcomes according to donor maximal AST.

Variables	Max. AST <475 UI *N* = 1190	Max. AST ≥475 UI *N* = 63	*P*
Maximal AST values	55 (6–473)	790 (478–2000)	
Recipient			
Recipient age, years	53 (12–74)	54 (13–70)	0.514
Recipient sex (male)	787 (66.1)	48 (76.2)	0.130
Recipient weight, kg	71 (30–172)	75 (43–126)	0.008
Recipient height, cm	170 (85.0–193)	172 (147–185)	0.126
Recipient BMI, kg/m2	24.5 (11.4–46.8)	25.9 (15.1–39.2)	0.007
MELD score	18.1 (6–40)	21.8 (6–40)	0.314
Medical situation at the time of LT			0.180
Home	777 (65.3)	44 (69.8)	
Hospital	239 (20.1)	7 (11.1)	
Intensive care unit	174 (14.6)	12 (19.0)	
Donor			
Donor age, years	57.5 (7–93)	49.0 (12–82)	<0.001
Donor age ≥80 years	111 (9.3)	1 (1.6)	0.061
Donor sex (male)	664 (55.8)	37 (58.7)	0.744
Donor weight, kg	72.5 (24–153)	75.0 (50–124)	0.119
Donor height, cm	170 (108–200)	172 (150–190)	0.008
Donor BMI, kg/m^2	24.9 (10.7–68.6)	25.6 (18.2–38.5)	0.739
Hypertension	448 (38.4)	11 (18.3)	0.003
Diabetes	113 (9.88)	1 (1.64)	0.055
Alcohol abuse	204 (17.1)	11 (17.5)	>0.99
Tobacco	423 (35.5)	31 (49.2)	0.039
Coronary arterial disease	106 (9.1)	8 (12.9)	0.431
Renal insufficiency	61 (5.3)	2 (3.2)	0.767
Cause of death			<0.001
Anoxia	148 (12.4)	42 (66.7)	
Others	29 (2.44)	2 (3.17)	
Trauma	318 (26.7)	6 (9.52)	
Stroke	695 (58.4)	13 (20.6)	
ICU stay, days	2 (0–62)	3 (1–24)	0.010
Cardiac arrest before donation	284 (23.9)	49 (79)	<0.001
Cardiac arrest duration, min	0 (0–120)	16.5 (0–90)	<0.001
Macrosteatosis ≥30%	30 (2.6)	2 (3.3)	0.671
Graft weight, g	1350 (530–4000)	1410 (700–2150)	0.489
Donor Risk Index*	1.60 (0.88–2.86)	1.32 (0.88–2.59)	<0.001
Donor Quality Index**	1.72 (1.00–2.8)	1.27 (1.00–2.10)	<0.001
First GGT, UI/l	30 (2–1147)	52 (10–492)	<0.001
Last GGT, UI/l	31 (2–1039)	56 (9–1333)	<0.001
LT & outcomes			
Cold ischemia time, min	479 (60.0–1019)	498 (233–974)	0.483
Length of surgery, min	561 (176–1300)	560 (325–1188)	0.947
No. of RBC	5 (0–73)	5 (0–45)	0.250
Postop. AST Peak, UI/l	1013 (11–25234)	863 (115–20574)	0.187
Serum INR at day 7	1.27 (0.58–8.0)	1.22 (0.95–2.03)	0.164
Serum bilirubin at day 7, µmol/l	40 (5–675)	48 (6–305)	0.955
Early Allograft Dysfunction***	460 (39.5)	17 (27.0)	0.549
Death or ReLT within 14 days	51 (4.3)	2 (3.2)	>0.99
Death or ReLT within 90 days	94 (7.9)	5 (7.9)	>0.99

BMI, Body mass index; ICU, Intensive care unit; INR, International Normalized ratio; RBC Red blood cell; ReLT, retransplantation; DRI, Donor Risk Index. *Donor Index: high value indicates poor quality or high risk; **Donor quality index according to Winter *et al*. [18]; ***Defined according to Olthoff *et al*.

Continuous variables are expressed as median (range). Categorical variables are expressed as absolute number (percentage).

Transplant International 2021; 34: 2247–2256

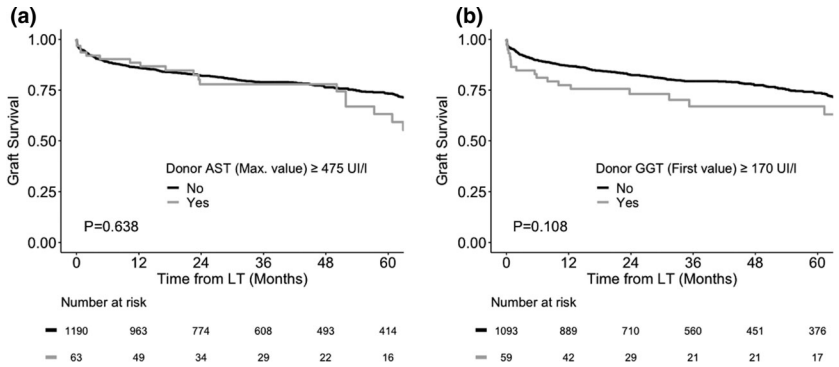

Figure 4 Kaplan–Meier graft survival curves according to 95th percentile of donor AST and donor GGT.

significantly lower when donor had a history of HAA (61% vs. 86%, $P = 0.033$). Surgical liver biopsy was available for 57 of grafts. Abnormal histological findings and steatosis were observed where more often in grafts from donors with HAA.

Discussion

Markedly increased AST and GGT are often observed in deceased donors. Assessing their prognostic significance is crucial for guiding the decision to accept or deny a hepatic graft. In this study, we found that donor AST and GGT were significantly associated with an increased risk of graft dysfunction, 90-day graft failure, and one-year graft survival. However, the risk remains limited and the use of these graft in routine is acceptable, given the current organ shortage.

The feasibility of transplanting livers from donors with elevated transaminases has already been documented. The one-year survival rates of 24 patients who received grafts from donors with transaminases ≥500 UI/l were similar to that of a control group, including 834 patients [14]. Another group also showed good results in a series of 8 transplantations after a strict selection applied on 15 grafts [15]. In the present study, a decrease of transaminases over time, suggesting recovery of liver injury, was required before considering graft acceptance. However, grafts from high AST donors had lower donor risk index and were recovered in younger donors, which reflect a clear selection bias. Retrospectively, we were more akin to accept grafts from high AST donor in the absence of additional risk factors. Therefore, the use of grafts with high AST is safe, provided favorable kinetics and no additional adverse factors.

The prognostic value of donor GGT is controversial. Donor GGT was an independent risk factor in the European donor risk index [16] but not in the former donor risk index [17], neither in the donor quality index [18] nor in the graft risk index [19]. GGT is not always mentioned in the definition of extended donor criteria [20, 21] and was not retained in the discard risk index [1]. Despite lower donor risk index and "gut feeling" selection by the recovery surgeon, grafts from donors with first GGT ≥170 UI/l yield lower graft survival at 90 days. Nevertheless, the one-year graft survival rate was not affected, thus indicating the risk of these grafts is mostly present at the early post-transplant period.

To better understand the relationship between donor AST and GGT and outcomes, we tested interactions with other variables and significant interaction with donor HAA. It appears that increasing donor GGT or AST correlates graft survival among donors with HAA whereas their values have no impact on outcomes when donors have no HAA. These findings have practical implications because deceased donors often present with a HAA, with a prevalence ranging from 12 to 18% [22–24]. A previous HAA should be looked for in donors with high GGT or AST. Although grafts from donors with HAA can be used safely as previously shown [22, 23], our results urge to be cautious when HAA is associated with high GGT or AST.

Whether the decision should be based on the first, maximal, or last value, is a question that could not be addressed here, given that the first GGT value was considered to be the most discriminative. Our rationale for giving priority to the first value relied on the fact that donor GGT level usually rises during a prolonged stay in intensive care unit, favored by drugs, artificial nutrition, or sepsis. On the contrary, an elevation of GGT at admission in ICU is suggestive of chronic liver disease, although numerous other etiologies should be considered.

Death or graft loss after LT is usually the result of several consecutive events worsened by poor general status of the recipient and can be rarely attributed to the sole graft quality. Poor grafts are usually discarded by the surgeon in charge of organ retrieval. We found that abnormal

Table 3. Comparisons of recipient, donor, and outcomes according to donor first GGT value.

Variables	First GGT <170 UI/l *N* = 1093	First GGT ≥170 UI/l *N* = 59	*P*
First GGT, UI/l	29 (2–169)	266 (170–1147)	
Recipient			
Recipient age, years	53 (12–73)	55 (20–74)	0.218
Recipient sex (male)	718 (65.7)	42 (71.2)	0.467
Recipient weight, kg	72 (30–172)	77 (35–126)	0.164
Recipient height, cm	170 (85–193)	170 (150–192)	0.535
Recipient BMI, kg/m^2	24.7 (12.5–44.2)	25.1 (11.4–46.8)	0.230
MELD score	18.5 (6–40)	18.7 (6–40)	0.616
Medical situation at the time of LT			0.248
Home	715 (65.4)	33 (55.9)	
Hospital	215 (19.7)	13 (22.0)	
Intensive care unit	163 (14.9)	13 (22.0)	
Donor			
Donor age, years	57.9 (7.6–93)	54.0 (19–84)	0.162
Donor age ≥80 years	103 (9.4)	2 (3.4)	0.181
Donor sex (male)	616 (56.4)	31 (52.5)	0.659
Donor weight, kg	72 (24–150)	80 (53–124)	0.039
Donor height, cm	170 (108–200)	170 (142–188)	0.973
Donor BMI, kg/m^2	24.9 (10.7–68.6)	26.2 (18.3–38.3)	0.012
Hypertension	405 (37.8)	23 (39.7)	0.887
Diabetes	105 (10.0)	3 (5.17)	0.326
Alcohol abuse	181 (16.6)	21 (35.6)	<0.001
Tobacco	384 (35.1)	29 (49.2)	0.041
Coronary arterial disease	108 (10.1)	4 (6.78)	0.545
Renal insufficiency	59 (5.56)	2 (3.57)	0.764
Cause of death			0.301
Anoxia	162 (14.8)	14 (23.7)	
Others	25 (2.29)	1 (1.69)	
Trauma	278 (25.4)	12 (20.3)	
Stroke	628 (57.5)	32 (54.2)	
ICU stay, days	2 (1–62)	6 (1–26)	<0.001
Cardiac arrest before donation	291 (26.7)	19 (32.2)	0.437
Cardiac arrest duration	0 (0–120)	0 (0–54)	0.318
Macrosteatosis ≥30%	27 (2.5)	1 (1.7)	>0.99
Graft weight, g	1350 (550–4000)	1645 (995–2320)	<0.001
European DRI*	1.59 (0.88–2.86)	1.47 (0.91–2.20)	0.05
Donor quality index**	1.72 (1.00–2.83)	1.35 (1.00–2.27)	<0.001
Last GGT, UI/l	31 (2–1039)	252 (91–1333)	<0.001
Maximal AST, UI/l	56 (6–2000)	120 (23–2000)	<0.001
LT & outcomes			
Cold ischemia time, min	483 (76–974)	457 (150–716)	0.382
Length of surgery, min	559 (176–1267)	547 (291–1033)	0.875
No. of RBC	5 (0–73)	6 (0–46)	0.071
Postop. AST Peak, UI/l	989 (11–25234)	1332 (252–20574)	0.029
Serum INR at day 7	1.26 (0.85–3.30)	1.23 (1.01–3.37)	0.111
Serum bilirubin at day 7, µmol/l	40 (5–675)	52 (12–457)	0.055
Early allograft dysfunction***	414 (38.7)	29 (49.2)	0.141
Death or ReLT within 14 days	42 (3.8)	4 (6.8)	0.290
Death or ReLT within 90 days	82 (7.50)	9 (15.3)	0.044

BMI, Body mass index; ICU, Intensive care unit; INR, International Normalized ratio; RBC Red blood cell; ReLT, retransplantation; DRI, Donor Risk Index; *Donor index: high value indicates poor quality or high risk; **Donor quality index according to Winter *et al*. [18]; *** defined according to Olthof *et al*.

Continuous variables are expressed as median (range). Categorical variables are expressed as absolute number (percentage).

Transplant International 2021; 34: 2247–2256

Table 4. Grafts from donors with high GGT: comparisons according to donor HAA.

Variables	No HAA $N = 38$	HAA $N = 21$	P
EAD	15 (39%)	14 (67%)	0.084
ReLT for graft non-function	0 (0%)	2 (10%)	0.123
Death at 30 days	2 (5%)	3 (14%)	0.337
Death or ReLT at 30 days	3 (8%)	5 (24%)	0.119
Death at 90 days	3 (8%)	3 (14%)	0.656
Death or ReLT at 90 days	4 (11%)	5 (24%)	0.258
Death at one year	4 (11%)	6 (29%)	0.144
Death or ReLT at one year	5 (14%)	8 (38%)	0.047
One-year graft survival, %	86%	61%	0.033
Main cause of death			
Sepsis	3	4	
Cardiovascular	1	1	
surgical complication	0	1	
End-LT liver biopsy*	No HAA $N = 37$	HAA $N = 20$	P
Fibrosis†	5 (13%)	5 (25%)	0.298
Necrosis	6 (16%)	4 (20%)	0.728
Neutrophils infiltration	11 (31%)	10 (53%)	0.190
Steatosis	9 (24%)	13 (65%)	0.006
Abnormal histology	16 (43%)	15 (79%)	0.024

EAD, early allograft dysfunction (Olthoff definition; ReLT, retransplantation).

*No biopsy available for 2 patients.

†No severe fibrosis was found.

histological findings and steatosis were common in presence of high GGT and donor HAA. Our results do not allow us to ascertain a direct relationship between donor GGT and graft survival but we can hypothesize that suboptimal graft quality may have affected organ function recovery, thus participating to initiate the cascade of complications leading to worse outcomes.

In addition to its retrospective and monocentric nature, this study carries some limitations. We analyzed only transplanted grafts and have no data about grafts that were declined at the time of the offer. Another limitation is that the drinking pattern could not be analyzed. This latter point is of importance because details of the donor drinking history are likely to improve the prediction of outcomes. The main strength of this study is that our selection policy concerning donor AST and GGT remained constant over time. As a consequence, the prognostic value of donor GGT or AST measured at other timings is affected by selection bias and interpretation is not warranted. We also acknowledge that risk of type I error (false positive) cannot be excluded because multiple tests have been performed. For that reason, other studies are needed to confirm our results.

In conclusion, safe transplantation of a graft from donors with high AST or GGT is possible under certain conditions, even though utmost caution is needed in donors with a drinking history. In these cases, a liver biopsy before organ recovery should be discussed to avoid futile organ recovery [25]. Viability assessment with *ex vivo* normothermic perfusion could be another option [26, 27].

Authorship

RC, ML, and MAA: designed the study and performed the research. YK, VK, and DDS: collected data. RC, ML, and MAA: wrote the manuscript. DC, DA, EV, RA, ASC, and NG: contributed important reagent.

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Conflicts of interest

The authors declare no conflict of interest.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. 3-month graft survival according to AST donor value (S1A. First value; S1B. Last value) and GGT donor value (S1C. Maximum value; S1D Last value).

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