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The impact of perceived donor liver quality on post-transplant outcome

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Key words
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Abstract

Background: We analysed the impact of perceived liver donor quality on transplant recipient outcomes.

Methods: this prospective cohort study included all deceased liver donors during 2008–2018 in the Swiss Transplant Cohort Study. Perceived low-quality liver donors were defined when refused for ≥5 top listed recipients or for all recipients in at least one centre before being transplanted. The effect of liver donor quality on relisting or recipient death at 1 week and 1 year after transplantation was analysed using Kaplan–Meier and Cox proportional hazard models. A 1:3 matching was also performed using a recipient score.

Results: Of 973 liver donors, 187 (19.2%) had perceived poor-quality. Males, obesity, donation after circulatory death and alanine aminotransferase values were significantly associated with perceived poor-quality, with no significant effect of the perceived quality on re-listing or death within the first week and first year post-transplant [(aHR) = 1.45, 95% CI: (0.6, 3.5), $P = 0.41$ and aHR = 1.52 (95% CI 0.98–2.35), $P = 0.06$], adjusting by recipient age and gender, obesity, diabetes, prior liver transplantation and model for end-stage liver disease (MELD) score. At 1 year, prior liver transplantation and higher MELD score associated with higher risk of re-listing or death.

Conclusion: Comparable post-transplant outcomes with different perceived quality liver donors stresses the need to improve donor selection in liver transplantation.

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Introduction

Liver transplantation remains the therapy of choice for end-stage liver disease. Its main limitation worldwide is donor organ shortage, precluding access to transplantation for waitlisted patients.[1]

Several strategies have been proposed to expand the donor pool, such as utilizing normothermic or hypothermic machine perfusion, particularly in more marginal donors. While this is a promising new strategy, it remains unavailable for many transplant centres and must as yet be established in widespread standard clinical practice.[2] Thus, increasing the use of available organs by expanding donor acceptance criteria is still of paramount importance. Marginal donors are defined as those with characteristics historically associated with higher risk of poor graft and patient survival[3,4] or with the potential transmission of a donor-derived disease.[5] Wider use of marginal donors is based on acceptable outcomes in recent years after changes in allocation policies, recipient characteristics as well as improvements in surgical techniques and donor/recipient matching.[6–9] Nevertheless, an accepted definition of what qualifies as a 'marginal donor' still needs to be defined.[3,10] Several scores have been proposed more than a decade ago to quantify donor quality in order to predict recipient outcomes, but none has been widely accepted.[11] Acceptance of a liver donor depends primarily on the perception of the liver donor quality, as assessed by the transplant team, combined with some known risk factors, such as degree of steatosis and cold ischaemia time. While the use of extracorporeal organ perfusion techniques to improve graft characteristics become increasingly implemented in daily use, assessment of graft function and evaluation of possible early post-transplant outcome remains challenging. In the end, perceived organ quality as assessed by the transplant team still prevails.

The focus of this study was to analyse the impact of perceived liver donor quality on transplant recipient outcomes. These results may allow optimizing donor acceptance criteria and organ allocation, which may have a significant impact on improving waiting list survival in countries such as Switzerland with low donation rates.

Methods and materials

Study design and data source

We performed a non-interventional study nested in the Swiss Transplant Cohort Study (STCS), a prospective nationwide observational cohort study enrolling patients undergoing solid organ transplantation in Switzerland since May 2008.[12] Donor information was retrieved from the Swiss Organ Allocation System (SOAS) with permission of Swisstransplant, who manage the donor data on a national basis. Data from liver transplant recipients were obtained from the STCS. In the STCS, demographic, clinical and laboratory data from solid organ transplant recipients are prospectively collected regularly at time of transplantation, 6- and 12-months post-transplant, and yearly thereafter. The study was conducted per the Declaration of Helsinki and Good Clinical Practice. Cantonal Ethics Committee (KEK-ID 2019-01040), as well as the Swiss Transplant Cohort Study approval (FUP 162), was obtained. The STCS is registered in the NIH clinicaltrials.gov (https://clinicaltrials.gov/ct2/show/NCT01204944). All transplant recipients included in the present study have given their written informed consent.

Study population

We considered all deceased liver donors registered in SOAS and their associated recipients transplanted in one of the three Swiss liver transplant centres (Bern, Zurich and Geneva) between 05/2008 and 12/2018. Follow-ups for recipients were considered until the end of 2019, but for a maximum of 1-year after transplantation (censoring). Living donations were excluded, as well as liver allografts exported for transplantation abroad. Transplants performed with foreign livers were included only if donor data were available. In total, 1043 deceased liver donors were registered during the study period; 70 donors were excluded due to incomplete recipient data post-transplant leaving 973 deceased liver donors and their related recipients for evaluation In addition to donor quality and demographic donor data, information on causes of donor death, type of deceased donation, cold ischaemic time and use of hypothermic oxygenated machine perfusion was included. Demographic recipient data was complemented by information on the urgency status of a transplant, the underlying liver disease leading to transplantation and liver transplantation history.

Definitions

We distinguished between 'perceived low quality liver donors (LD)' and 'perceived standard quality LD'. A 'perceived low-quality LD' was defined as a donor that was refused for at least the top-listed five recipients or refused for all recipients in at least one centre and then transplanted in another recipient on a national basis. LD who did not meet these criteria were considered as perceived standard quality LD.

Switzerland has three liver transplant centres and one national waiting list managed by Swisstransplant. Allocation is patient-based.[13] In the setting of a super-rapid donation after circulatory death (DCD) liver retrieval, organ perfusion is done using the HOPE technique (hypothermic, oxygenated), with all three centres using the same machine. While most of such DCD livers will be perfused using hypothermic oxygenated machine perfusion, it is up to the discretion of the surgeon to decide if this is done. DCD livers explanted using normothermic regional perfusion (carried out in one single hospital in Switzerland) do not undergo additional hypothermic machine perfusion.

The primary endpoint of this study was to analyse liver transplantation outcomes (re-listing for liver transplantation or patient mortality as a composite outcome) during the first week and first year after liver transplantation in patients who received a perceived low quality versus standard quality donor liver. Secondary endpoints were to describe and compare the characteristics of liver donors to predict which associated with the definition of perceived low quality, as well as describing and comparing the characteristics of candidates who received these types of donor livers.

Statistical analysis

We performed a descriptive analysis for donor and recipient characteristics regarding perceived low and standard quality LD. Quantitative and categorical variables were expressed as median and interquartile range, and percentages, respectively. Logistic regression models were used to identify donor variables predicting low-quality LD.

The effect of LD quality on the time to one-week and one-year study endpoints (relisting or recipient death) was analysed using Kaplan–Meier method and Cox proportional hazard models. We estimated the event-free survival time as time from transplantation until the composite endpoint of re-listing, recipient death or censoring, whichever occurred first. As mentioned in the literature, we considered the following information indispensable for prediction: donor age, DCD, and split donation, recipient age, their urgency for transplantation and their calculated model for end-stage liver disease (MELD) score at transplantation. Due to a strong association between DCD and machine perfusion (85 of 89 DCD donors had machine perfusion) one of both variables was included in multivariate models to avoid collinearity.

As complementary analysis, a 1:3 matching using a recipient score was performed, to assess the intrinsic quality of liver grafts by accounting for the recipient covariates that may influence post-transplant outcomes.[14,15] This score was defined considering recipient age, gender, and body mass index (BMI) as well as previous diabetes exposure, hepatocellular carcinoma (HCC) as underlying cause for liver transplantation and MELD at time of transplantation. Recipients with perceived low-quality LD were matched with recipients with perceived standard-quality LD. An optimal matching method was applied to minimize average recipient score across all matched sets.

All tests were two-sided and significance level was set to 5%. STATA (StataCorp., version 14.2) and R software (version 4.0.4) were used for statistical calculations.

Results

Characteristics and perceived quality of liver donors

We identified 187 (19.2%) donors that fitted the definition of perceived low-quality LD. The majority of perceived low-quality LD were refused for the first five-top listed candidates (108/187, 57.8%) (no further data regarding the cause of rejection). The remaining liver donors were rejected for all candidates in at least one Swiss liver transplant centre, due to perceived low quality (77/79) or logistical reasons (2/79).

Cerebrovascular disease was the most frequently reported cause of death, which prevailed in standard-quality LD, followed by anoxia, prevalent in low-quality LD. Donors perceived as low-quality LD were older, more often male, obese, diabetic and showed higher aspartate aminotransferase and alanine aminotransferase (ALAT) values (Table 1). Additionally, the proportion of donors with a history of alcohol consumption was higher in perceived low-quality LD. Regarding serology, 10 donors (1%) had positive serology for hepatitis B (HBsAg or anti-Hb core positive) or hepatitis C (anti-HCV positive).

Split donors were more frequently perceived as standard-quality LD, whereas DCD was more frequently observed in low-quality LD.

In 85 donors, hypothermic oxygenated machine perfusion was administered after procurement. Of note, this technique was applied in only 1.7% of patients identified as standard quality liver donors and 38.5% of perceived low quality liver donors (Table 1).

In a final multivariable model, male donors, obese donors, DCD and higher ALAT values were found to significantly increase the probability of being perceived as having low liver quality (Table 2).

Recipient characteristics and post-transplant outcomes

Recipients were middle aged, and more often men. Their main indication for liver transplantation was HCC. Patients who received a perceived low-quality LD were more often male, older, with a diagnosis of diabetes and HCC as an indication for liver transplantation (Table 3). On the contrary, patients who received a standard-quality LD more often had higher MELD scores at liver transplantation or were listed for a re-transplantation. Overall, only 5% of all patients were listed under urgency status, all of whom received a perceived standard quality LD.

Within the first week post-transplant, 32 events were observed: 17 patients were re-listed and 15 died. Event-free survival at one-week was 96.3% and 96.8% in recipients with perceived low-quality (7/187) and standard-quality donor livers (25/786) respectively (Fig. 1). When considering the first year after liver transplantation, 129 events were observed: 79 patients died, and 50 liver recipients were re-listed for liver transplantation. Survival without need for re-listing after one-year post-transplantation was 85% and 87.2% in recipients with perceived low and standard quality liver donors respectively (Fig. 2).

There was no significant effect of the perceived liver donor quality on the need for re-listing or patient's death within the first week post-transplant [adjusted hazard ratio (aHR) = 1.45, 95%-confidence interval (CI): (0.6, 3.5), $P = 0.41$], considering relevant recipient characteristics such as recipient age and gender, obesity and diabetes status, previous liver transplantation and MELD at transplantation (Table 4, left).

Similarly, when analysing re-listing or death of the patient within the first year after transplantation, only prior liver transplantation ($P = 0.005$) and a higher MELD score at the time of transplantation ($P = 0.004$) had a clear influence (Table 4, right).

Based on the matching approach, both 1-week and 1-year results were confirmed, although we observed a bordeline significant value in the latter (Table 4, bottom).

Relevant recipient characteristics were balanced between patients receiving low and standard liver donor quality in the matched sample (Table 5).

Focusing on the effect of the detailed donor characteristics rather than on the perceived liver quality when assessing recipient outcome, donor type also proved to be an important predictor of

Table 1 Description of liver donor and peri-transplant characteristics according to the perceived donor quality

Donor characteristics	All donors ($n = 973$)	Standard quality donors ($n = 786$)	Perceived low quality donors ($n = 187$)
Age (median, IQR)	55 (43–67)	55 (41–66)	58 (45–70)
<40 years—*n* (%)	216 (22.2)	181 (23)	35 (18.7)
40–60 years—*n* (%)	379 (39)	316 (40.2)	63 (33.7)
61–70 years—*n* (%)	196 (20.1)	153 (19.5)	43 (23)
>70 years—*n* (%)	182 (18.7)	136 (17.3)	46 (24.6)
Gender (male)—*n* (%)	549 (57)	426 (54.9)	123 (65.8)
Obesity (BMI ≥ 30)—*n* (%)	105 (10.8)	73 (9.3)	32 (17.1)
Diabetes—*n* (%)	71 (7.3)	46 (5.9)	25 (13.4)
Alcohol history—*n* (%)	440 (45.2)	341 (43.4)	99 (52.9)
Cause of death			
Anoxia—*n* (%)	229 (23.5)	170 (21.6)	59 (31.6)
CVD—*n* (%)	512 (52.6)	424 (53.9)	88 (47.1)
Trauma—*n* (%)	200 (20.6)	164 (20.9)	36 (19.3)
Other—*n* (%)	32 (3.3)	28 (3.6)	4 (2.1)
DCD—*n* (%)	89 (9.1)	15 (1.9)	74 (39.6)
Machine perfusion—*n* (%)	85 (8.7)	13 (1.7)	72 (38.5)
Split donor—*n* (%)	59 (6.1)	50 (6.4)	9 (4.8)
ASAT (max)—median, IQR	64 (33–164)	63 (32–158)	80 (38–241)
ALAT (max)—median, IQR	40 (22–115)	39 (22–105)	61 (23–186)
Serum sodium (max) median, IQR	148 (144–152)	148 (144–152)	148 (143–152)
Days in ICU prior to donation—median, IQR	2 (2–4)	2 (2–3)	3 (2–5)
Cold ischaemia time (hours)	7 (5–8)	7 (5–8)	7 (6–8)

Abbreviations: ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; BMI, body mass index; CVD, cerebrovascular disease; DCD, donation after circulatory death, ICU, intensive care unit.

Table 2 Effect estimates for donor information from logistic regression models predicting perceived low donor quality

	OR 95% CI *P* value	
Donor characteristics	Univariate	Multivariable*
Age at donation (years)	1.01 (1.00, 1.02) 0.02	1.01 (0.99, 1.02) 0.19
Gender: male versus female	1.58 (1.13, 2.2) 0.007	**1.58 (1.06, 2.38) 0.03**
Obesity (BMI ≥30)	2.02 (1.29, 3.16) 0.002	**2.60 (1.54, 4.38) < 0.001**
Diabetes	2.48 (1.48, 4.16) <0.001	1.85 (0.96, 3.54) 0.07
Alcohol history	1.47 (1.07, 2.02) 0.02	1.07 (0.72, 1.58) 0.74
Death cause: anoxia	1.67 (1.17, 2.38) 0.03	0.75 (0.46, 1.25) 0.27
Split donor	0.74 (0.36, 1.54) 0.43	–
DCD	**33.66 (18.68, 60.67) < 0.001**	**34.50 (18.52, 64.29) < 0.001**
Machine perfusion	**37.23 (20.00, 69.36) < 0.001**	
Cold ischaemia (hours)	1.04 (0.96, 1.13) 0.31	–
ASAT max (UI/ml)	**1.0007 (1.0003, 1.0012) 0.003**	–
ALAT max (UI/ml)	**1.001 (1.0004, 1.0016) 0.001**	**1.001 (1.0006, 1.0021) 0.001**
Serum sodium (mg/dl)	0.99 (0.97, 1.02) 0.47	–

Note: Missing values were in donor gender (10) and ALAT max (2). Bold values are those with significant *p* values.

Abbreviations: ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; BMI, body mass index; DCD, donation after circulatory death.

*961 patients with complete information were included.

recipient outcome at 1-week and at 1-year (Table 6). In addition, a split liver and older age of the donor proved to have a negative influence on the one-year outcome ($P < 0.05$).

Discussion

In this cohort study that analysed all deceased liver donors and their associated recipients transplanted in Switzerland during a 10-year period we found that almost 20% of liver donors were perceived as low quality. However, these donors were not associated with a higher risk of relisting or death during the first week or first year after transplantation, even when adjusting for relevant recipient characteristics.

Liver donor quality is defined as a continuum of risk rather than a dichotomous definition of good or bad quality donors.[5] Despite the fact that several donor variables have been associated with poor graft survival, such as macrosteatosis, advanced donor age, split donation or DCD, variables which have been integrated in donor risk scores,[16,17] these tools have not reached widespread use, mainly due to lack of regional validation.[11] Thus, upon a donor offer, the assessment of graft quality is still mainly based on the transplant team's experience and their perception of risk for the given recipient.[4]

A surrogate of a perceived low quality liver donor is the rejection rate for top-listed candidates before the final acceptance of the graft. The number of rejections even modifies allocation policies in some countries: after being discarded by three teams in Germany or five teams in France, the liver is considered for centre allocation (also called rescue allocation), and thus the transplant program that finally

Table 3 Description of liver transplant recipients according to the perceived liver donor quality

	Total $n = 973$	Perceived standard quality donors ($n = 786$)	Perceived low quality donors ($n = 187$)	*P*-value
Age at LT (yrs), median (IQR)	56 (47–62)	56 (47–62)	57 (51–62)	0.009
Gender (male), *n* (%)	695 (71.4)	550 (70)	145 (77.5)	0.040
Obesity (BMI ≥30), *n* (%)	188 (19.6)	147 (19)	41 (21.9)	0.373
Diabetes, *n* (%)	253 (26)	192 (24.4)	61 (32.6)	0.022
HCC as indication for LT, n (%)	439 (45.2)	335 (42.7)	104 (55.6)	0.002
LT history, *n* (%)	89 (9.1)	83 (10.6)	6 (3.2)	0.003
Calculated MELD at LT, median (IQR)	14 (8–23)	14 (8–25)	13 (8–18)	<0.001

Abbreviations: BMI, body mass index; HCC, hepatocellular carcinoma; LT: liver transplantation; MELD, model for end-stage liver disease.

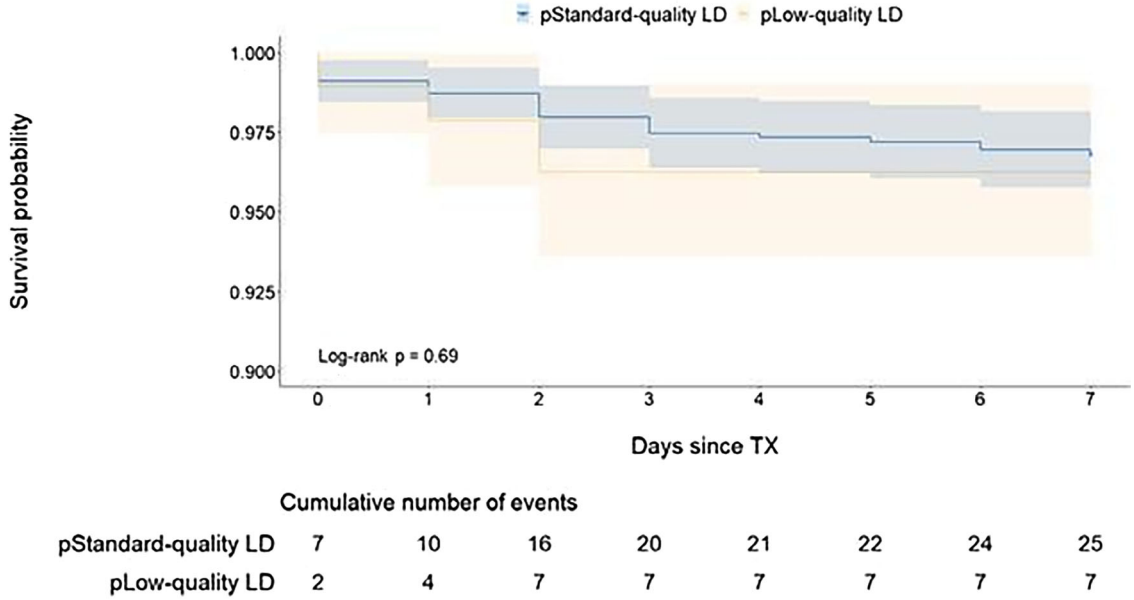

Fig. 1. Liver donor quality and re-listing/mortality during the 1st week after liver transplantation. pStandard-quality LD: perceived standard quality liver quality, pLow-quality LD, perceived low-quality liver donors. TX, transplantation. The coloured area above and below the Kaplan Meier curves represents the 95% confidence interval.

accepts the organ can freely choose the recipient on their waiting list.[18–20] In our study cohort, 19.2% of transplanted candidates received a liver donor that fulfilled our definition of perceived poor liver quality. These rates are consistent with other European series, where the use of previously discarded donors ranged between 8.2% and 34%.[21,22] Several variables were associated with the perception of low quality, such as male gender, obesity (likely as a surrogate of liver steatosis), higher transaminase values and DCD as donor type. However, only DCD correlated with post-transplant recipient outcomes, as well as donor age and split donors. The latter were not associated with the perception of poor quality but extensively reported to be associated with graft survival.[16]

Notably, perceived low quality liver donors were not associated with worse graft or recipient outcomes during the first week or first year after liver transplantation, when compared to standard quality donors. These results are consistent with reports from the UK and France that found comparable short- and long-term survival outcomes between rescue allocation and standard allocation liver donors.[19,21,23]

It can be argued that these comparable results were achieved due to a careful donor and recipient matching. In this cohort, perceived low quality liver donors were more frequently allocated to less severely ill recipients, such as those undergoing a first liver transplantation, with lower MELD scores and with HCC as the underlying aetiology. These findings are in line with the traditional and widely accepted approach of balancing risk, that proposes that lower risk recipients will tolerate a poor-quality liver graft better, whereas sicker patients would benefit more from receiving a good quality donor.[7,24] However, comparable 1-week and 1-year outcomes were observed after matching for recipient co-variables that may have an impact on post-transplant outcomes, although borderline significant results at 1-year require to confirm these results in further studies.

Another relevant aspect to consider is the effect of hypothermic oxygenated machine perfusion in marginal donors. This technique aims at improving liver function by decreasing ischaemic damage, and thus optimizing graft and patient survival when using marginal liver grafts.[25] In a recently published randomized controlled trial

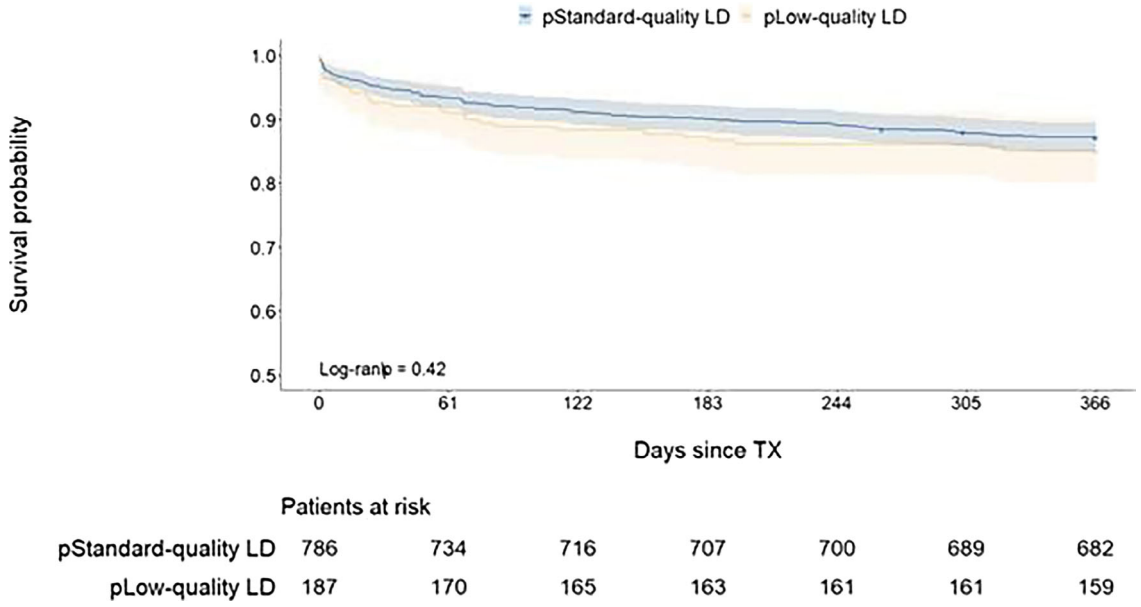

Fig. 2. Liver donor quality and re-listing/mortality during the 1st year after liver transplantation. pStandard-quality LD: perceived standard quality liver quality, pLow-quality LD: perceived low-quality liver donors, TX, transplantation.

Table 4 Effect estimates for recipient variables and liver donor quality from Cox proportional hazard models for recipient's outcome, at one-week and one-year post-transplant, and in the full and in a 1:3 matched sample

	One-week outcome		One-year outcome	
	HR (95%-CI) *P*-value	# patients [# events]	HR (95%-CI) *P*-value	# patients [# events]
Full sample				
Univariate	1.19 (0.51–2.74) 0.69		1.19 (0.78–1.81) 0.42	973 [129]
pLow-donor quality		973 [32]		
Multivariable[†]				
pLow-donor quality	1.45 (0.61–3.47) 0.41	957 [30]	1.52 (0.98–2.35) 0.06	957 [121]
Recipient age at LT (yrs)	1.01 (0.82–1.46) 0.53		1.16 (1.00–1.34) 0.05	
Recipient–male	1.37 (0.57–3.29) 0.49		0.96 (0.64–1.44) 0.83	
Diabetes	1.05 (0.47–2.33) 0.91		0.83 (0.55–1.26) 0.39	
Obesity (BMI > 30)	1.10 (0.44–2.78) 0.84		0.82 (0.50, 1.34) 0.42	
HCC diagnosis	0.74 (0.30–1.84) 0.52		0.84 (0.53–1.32) 0.44	
Calculated MELD at LT	1.01 (0.98–1.05) 0.48		**1.03 (1.01–1.05) 0.004**	
Re-LT status	2.41 (0.92–6.33) 0.07		**2.06 (1.25–3.39) 0.005**	
Matched sample (1:3)[‡]				
pLow-donor quality	1.52 (0.60–3.82) 0.38	748 [21]	1.65 (1.01–2.71) 0.05	748 [81]

Note: Bold values are those with significant *p* values.

Abbreviations: BMI, body mass index; HCC, hepatocellular carcinoma; HR, hazard ratio; LT, liver transplantation; MELD, model for end-stage liver disease; re-LT: re-liver transplantation.

[†]There were missing values in recipient variables: 'obesity' (14), 'HCC diagnosis' (2).

[‡]According to the matching design, 561 patients with pStandard-quality donors were matched to 187 patients with pLow quality donors.

Table 5 Description of recipient characteristics in the 1:3 matched sample

	Total ($n = 748$)	Perceived standard quality donors ($n = 561$)	Perceived standard quality donors ($n = 187$)
Age at LT (years), median (IQR)	57 (50–63)	57 (49–63)	57 (51–62)
Gender (male), *n* (%)	564 (75.4)	419 (74.7)	145 (77.5)
Obesity (BMI > 30), *n* (%)	153 (20.5)	112 (20)	41 (21.9)
Diabetes, *n* (%)	220 (29.4)	159 (28.3)	61 (32.6)
HCC diagnosis, *n* (%)	407 (54.4)	303 (54)	104 (55.6)
MELD at LT, median (IQR)	11 (8–18)	10 (8–18)	13 (8–18)
Re-LT status, *n* (%)	27 (3.6)	21 (3.7)	6 (3.2)

Abbreviations: BMI, body mass index; HCC, hepatocellular carcinoma; LT, liver transplantation; MELD, model for end-stage liver disease.

Table 6 Effect estimates for selected recipient and donor variables from multivariable Cox proportional hazard models for recipient's outcome, at 1 week and 1 year post-transplant, and in the full and in a 1:3 matched sample

	One-week outcome		One-year outcome	
	HR (95%-CI), *P*-value	# patients [# events]	HR (95%-CI), *P*-value	# patients [# events]
Full sample				
Recipient age at LT (yrs)	–	973 [32]	1.17 (1.001–1.36) 0.05	957 [121]
Recipient gender -male	–		1.00 (0.66–1.5) 0.99	
Recipient diabetes	–		0.76 (0.50–1.15) 0.19	
Recipient obesity	–		0.84 (0.51–1.37) 0.49	
HCC diagnosis leading to LT	–		0.76 (0.48–1.20) 0.24	
MELD at LT	–		1.03 (1.009–1.05) 0.004	
Recipient re-LT status	3.05 (1.31–7.09) 0.009		2.03 (1.23–3.35) 0.006	
Donor age at donation (yrs)	–		1.02 (1.003–1.03) 0.01	
Split donor	–		2.85 (1.30–6.28) 0.009	
DCD	2.55 (1.05–6.23) 0.04		2.47 (1.50–4.08) <0.001	
Machine perfusion[‡]	–		–	
Matched sample (1:3)				
Donor age at donation (yrs)	–	748[†] [21]	1.02 (1.003–1.03) 0.02	748 [81]
Split donor	–		3.21 (1.36–7.59) 0.01	
DCD	3.26 (1.26–8.38) 0.01		2.29 (1.35–3.9) 0.002	
Machine perfusion+	–		–	

[†]According to the matching design, 561 patients with pStandard-quality donors were matched to 187 patients with pLow quality donors.

[‡]Data not shown due to collinearity with DCD.

Abbreviations: HCC, hepatocellular carcinoma; DCD: donation after circulatory death; LT, liver transplantation; MELD: model for end-stage liver disease; re-LT: re-liver transplantation.

assessing its impact in extended criteria donation from brain dead donors, it was found to reduce early allograft injury and to improve intensive care unit stay and early complications in comparison with static cold storage.[26] In our study cohort, hypothermic oxygenated machine perfusion was used in almost 9% of the entire sample, and in more than one third of liver donors perceived as having poor liver quality. However, the use of machine perfusion yielded similar results as DCD grafts that did not receive this treatment; and due to comparable results and collinearity in data analysis, this variable was not included in the multivariable models shown. These results may suggest that machine perfusion could not ameliorate the impact of DCD donation on graft and recipient outcomes. However, it should be noted that our study did not primarily aim at analysing the impact of this treatment, and thus it may be underpowered to detect a possible benefit in graft or patient survival

The present study has several strengths, such as the analysis of data obtained from a nationwide cohort study that consecutively enrolled all patients with available post-transplant results, which allowed for the control and adjustment of several confounding covariates; as well as the analysis of a larger sample size than initially calculated, that diminishes the chance of a type II error. Our main limitations were related to the retrospective design and to the definition of perceived poor quality liver donor. We acknowledge this definition may be controversial, due to the lack of established consensus regarding which donor features negatively impact recipient outcomes. We have adopted a definition of perceived quality mainly based on prior refusals rather than in specific clinical features, to evaluate whether these refusals correlated with poor outcomes after transplantation. Of course, there might be other reasons besides perceived quality that influenced the decision to accept a specific donor, but we believe the rejection rate parallels the rescue allocation criteria considered in other countries for donors deemed marginal.

As previously suggested in Markov model analysis, the allocation of a perceived low quality liver donor could probably optimize the survival benefit particularly for sicker recipients.[27] The excellent and comparable post-transplant outcomes observed with perceived low quality LD stresses the need to re-evaluate the perception of LD quality and the benefit associated with their use in top-listed candidates.

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Author contributions

Melisa Dirchwolf: Conceptualization; formal analysis; investigation; methodology; resources; writing – original draft; writing – review and editing. **Chiara Becchetti:** Conceptualization; data curation; formal analysis; investigation; project administration; writing – original draft; writing – review and editing. **Susanne Stampf:** Formal analysis; methodology; software; validation; writing – review and editing. **Christa Haldimann:** Data curation; investigation; resources; validation; writing – review and editing. **Franz F. Immer:** Conceptualization; funding acquisition; project administration; supervision; validation. **Franziska Beyeler:** Data curation; investigation; project administration; supervision; validation. **Christian Toso:** Data curation; formal analysis; resources; validation; writing – review and editing. **Philipp Dutkowski:** Data curation; funding acquisition; project administration; supervision; validation. **Daniel Candinas:** Funding acquisition; investigation;

project administration; supervision; validation. **Jean-Francois Dufour:** Conceptualization; formal analysis; investigation; methodology; project administration; supervision; validation; writing – review and editing. **Vanessa Banz:** Conceptualization; data curation; formal analysis; investigation; project administration; supervision; validation; writing – original draft; writing – review and editing.

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Conflict of interest

None declared.

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