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Impact of Donor Cirrhosis Outcome Risk Estimator (CORE) Score on Recipient Outcomes Following Living-donor Liver Transplantation

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Abstract

Background/Aim: Several studies have investigated predictive factors for outcomes of living-donor liver transplantation (LDLT). However, few have examined the clinical significance of the Cirrhosis Outcome Risk Estimator (CORE) score on prognosis following LDLT. This study aimed to investigate the impact of donor CORE scores in predicting the outcomes of patients undergoing LDLT.

Patients and Methods: This single-center retrospective study included 362 adult LDLT recipients at our Institution between January 1998 and December 2024. Patient and graft survival rates were compared between the groups with low (≤0.05) and high (>0.05) CORE scores. Subsequently, multivariate analyses were performed to investigate prognostic factors for survival, including the CORE score.

Results: Patients in the group with a low CORE score had significantly better survival (p=0.001; 5-year, 85.3% *vs.* 76.2%) and graft survival (p=0.001; 5-year, 84.1% *vs.* 74.6%) than those with a high CORE score. Multivariate analyses identified the CORE score (>0.05) as an independent predictor of patient survival (hazard ratio=1.70, 95% confidence interval=1.01-2.62, p=0.018) and graft survival (hazard ratio=1.66, 95% confidence interval=1.07-2.57, p=0.024).

Conclusion: This study demonstrated the clinical significance of donor CORE scores in recipient outcomes after LDLT. Assessment of the donor CORE score may be useful for evaluating the quality of liver grafts and estimating recipient outcomes.

Keywords: Living-donor liver transplantation, donor, recipient, survival outcomes, Cirrhosis Outcome Risk Estimator score, CORE.

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Introduction

Liver transplantation is the only effective treatment for end-stage liver disease (1). Owing to the increased incidence of liver disease and organ shortages, living-donor liver transplantation (LDLT) is one approach that has been used to expand the donor pool (2, 3). Several studies have investigated the factors predictive of outcomes after liver transplantation, and donor characteristics have been recognized as important factors affecting outcomes after transplantation (4, 5). In deceased donor liver transplantation (DDLT), extended donor criteria, including donor age, steatosis, donation type, and ischemic time, have been used to evaluate liver graft quality (6, 7). However, the concept of extended-criteria donors for LDLTs remain unclear.

The Cirrhosis Outcome Risk Estimator (CORE) score is a novel model for stratifying patients at risk of liver disease in the general population (8). As the CORE score was developed using data from the general population, we hypothesized that it might be adopted to evaluate the quality of living-donor liver grafts and to predict recipient outcomes after LDLT. Therefore this study aimed to investigate the impact of the donor CORE score on recipient outcomes following LDLT.

Patients and Methods

Patients. This retrospective study included adult LDLT recipients who underwent LDLT at our Institution between January 1998 and December 2024. Pediatric and adult recipients who underwent DDLT were excluded. This study was approved by the Ethics Committee of Okayama University Hospital (approval no. 1911-028). The requirement for informed consent was waived because of the retrospective nature of the study.

Data collection. Donor data included age, sex, laboratory values, and graft type (right, right posterior, and left lobe) (9). The following recipient data were extracted: Age, sex, Child–Pugh score, Model for End-Stage Liver Disease (MELD) score (10), primary diseases (alcoholic, acute liver failure, viral hepatitis, hepatocellular carcinoma, metabolic, primary biliary cholangitis, primary sclerosing cholangitis, and others), ABO blood type (identical, compatible, and incompatible), operative time, estimated blood loss, and graft-to-recipient weight ratio (GRWR) (11).

CORE score and cut-off value. The donor CORE score was calculated using age, sex, γ-glutamyl transferase (U/l), aspartate aminotransferase (U/l), and alanine aminotransferase (U/l) (https://rickstra.shinyapps.io/CORE/) (8). Using the Youden index, the optimal cutoff value for the CORE score was determined (12). Subsequently, the recipients were divided into two groups based on their donor CORE scores.

Statistical analysis. Patient and graft survival rates were calculated using the Kaplan-Meier method, and differences between curves were analyzed using the log-rank test. Univariate and multivariate analyses were performed using a Cox proportional hazards model to identify the predictive factors for patient and graft survival. Variables with $p<0.15$ in the univariate analysis were included in the multivariate analysis. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated. Values are reported as proportions for categorical data and medians with interquartile ranges (IQR) for continuous variables. Statistical analyses were performed using the Mann-Whitney *U*-test for continuous variables and Fisher's exact test for categorical variables. Statistical significance was set at $p<0.05$. All statistical analyses were performed using JMP software version 11 (SAS Institute, Cary, NC, USA).

Results

Study cohort. After excluding pediatric (n=92) and adult recipients who underwent DDLT (n=70), 362 adult recipients who underwent LDLT were included. The characteristics of the 362 recipients and donors are presented in Table I.

There were 194 male and 168 female recipients, with a median age of 53 years (IQR=44-59 years). The median MELD

Table I. *Donor and recipient characteristics.*

	Variable		N=362
Donor	Age, years	Median (IQR)	40 (30-52)
	Sex, n (%)	Male	197 (54.4)
		Female	165 (45.6)
	γ-Glutamyl transferase, U/l	Median (IQR)	21 (15-32)
	Aspartate aminotransferase, U/l	Median (IQR)	19 (16-23)
	Alanine aminotransferase, U/l	Median (IQR)	18 (13-25)
	CORE score	Median (IQR)	0.07 (0.03-0.16)
	Graft type, n (%)	Right lobe	207 (57.2)
		Left lobe (with/without caudate)	142 (39.2)
		Right posterior	13 (3.6)
	Graft weight, g	Median (IQR)	610 (475-708)
Recipient	Age, years	Median (IQR)	53 (44-59)
	Sex, n (%)	Male	194 (53.6)
		Female	168 (46.4)
	Child–Pugh score, n (%)	A/B	105 (29.0)
		C	257 (71.0)
	MELD score	Median (IQR)	16 (13-21)
	Disease, n (%)	Alcoholic	37 (10.2)
		Acute liver failure	36 (9.9)
		HBV/HCV	75 (20.7)
		HCC	79 (21.8)
		Metabolic	20 (5.5)
		PBC/PSC	58 (16.0)
		Other	57 (15.7)
	ABO blood type, n (%)	Identical	243 (67.1)
		Compatible	87 (24.0)
		Incompatible	32 (8.8)
	Operative time, min	Median (IQR)	570 (498-635)
	Blood loss, l	Median (IQR)	4.6 (2.4-8.2)
	GRWR	Median (IQR)	1.04 (0.77-1.21)

CORE: Cirrhosis Outcome Risk Estimator; GRWR: graft-to-recipient weight ratio; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; HCV: hepatitis C virus; IQR: interquartile range; MELD: Model for End-Stage Liver Disease; PBC: primary biliary cholangitis; PSC: primary sclerosing cholangitis.

score was 16 (IQR=13-21). ABO blood type compatibility was identical for the majority of cases (n=243). The median operative time was 570 min (IQR=498-635 min), with a median blood loss of 4.6 l (IQR=2.4-8.2 l). The median donor age was 40 years (IQR=30-52 years) . The donor laboratory values were within the normal range, with a median CORE score of 0.07 (IQR=0.03-0.16) (Figure 1). The most common graft type was the right lobe (57.2%), followed by the left (39.2%).

Cut-off value of the donor CORE score. In this study, the optimal cut-off value for the donor CORE score was defined as 0.05. Recipients were divided into two groups based on their donor CORE score: low CORE score (score ≤0.05) and high CORE score (score >0.05).

Patient and graft survival. Patients in the group with a low CORE score had significantly better survival rates than those in the group with a high CORE score (p=0.001, Figure 2A). Following a median follow-up of 11.1 years (IQR=4.4-17.6 years), corresponding 5-, 10-, and 15-year patient survival rates were 85.3%, 82.0% and 79.3%, and 76.2%, 68.4% and 59.0%, respectively.

Graft survival was significantly better in the group with a low CORE score than in the group with a high CORE score (p=0.001; Figure 2B). The corresponding

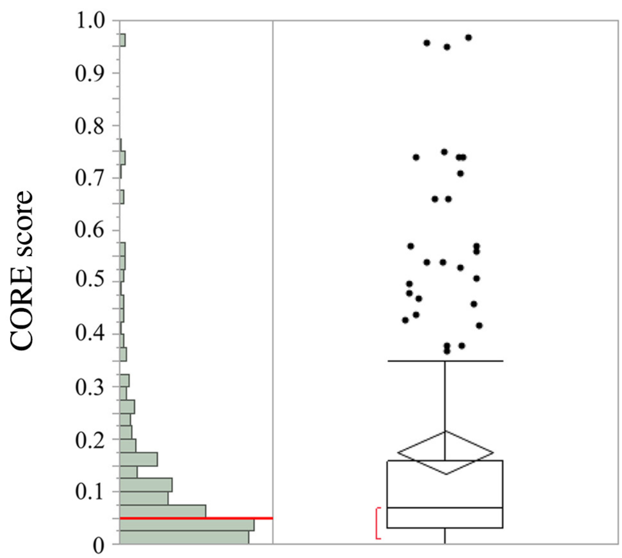

Figure 1. *Distribution of donor Cirrhosis Outcome Risk Estimator (CORE) scores. The box indicates the interquartile range, whiskers indicate the range, the line inside the box indicates the median value, and the diamond indicates the mean.*

5-, 10-, and 15-year graft survival rates were as follows: 84.1%, 80.7% and 78.1%, and 74.6%, 67.6% and 58.0%, respectively.

Prognostic factors after LDLT. The results of the univariate and multivariate analyses for identifying the prognostic factors for patient survival are summarized in Table II. In the univariate analysis, donor age (≥50 years) (HR=1.55, p=0.022) and CORE score (>0.05) (HR=1.85, p=0.001) were identified as prognostic factors associated with poorer patient survival. Multivariate analyses observed a CORE score >0.05 to be an independent predictor of poorer patient survival after LDLT (HR=1.70, 95% CI=1.01-2.62, p=0.018).

Table III shows the results of the univariate and multivariate analyses to identify the prognostic factors for graft survival. In the multivariate analyses, a CORE score >0.05 was identified as a significant factor associated with poorer graft survival (HR=1.66, 95% CI=1.07-2.57, p=0.024).

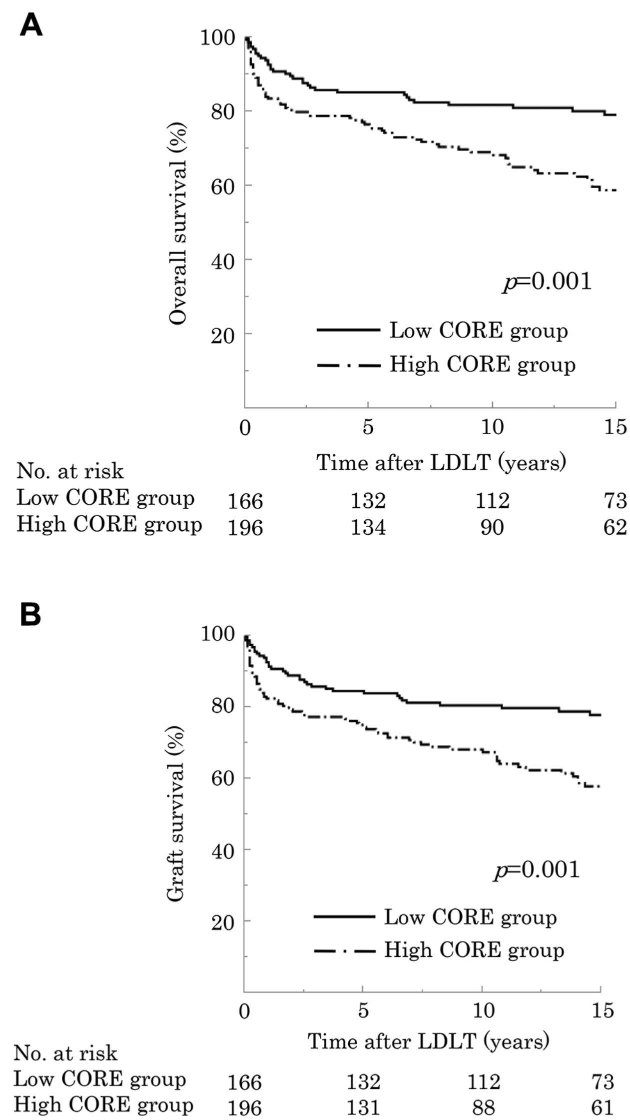

Figure 2. *Survival curves after living-donor liver transplantation (LDLT) according to Cirrhosis Outcome Risk Estimator (CORE) score. (A) Overall survival and (B) graft survival curves are shown.*

Discussion

To the best of our knowledge, this is the first study to investigate the effect of donor CORE scores on recipient outcomes after LDLT. The results showed that patients in the group with a CORE score <0.05 had significantly better patient and graft survival rates. Moreover, the donor CORE

Table II. *Univariate and multivariate analyses of prognostic factors associated with patient survival after living-donor liver transplantation (n=362).*

			Univariate			Multivariate		
Variable	Subgroup	n (%)	HR	95% CI	*p*-Value	HR	95% CI	*p*-Value
Donor age	≥50 years	109 (30.1%)	1.55	1.07-2.24	**0.022**	1.16	0.76-1.80	0.492
Donor sex	Male	197 (54.4%)	1.17	0.82-1.69	0.393			
CORE score	>0.05	196 (54.1%)	1.85	1.28-2.71	**0.001**	1.70	1.01-2.62	**0.018**
Recipient age, years	≥60 years	83 (22.9%)	1.21	0.79-1.79	0.377			
Recipient sex	Male	194 (53.6%)	1.15	0.81-1.66	0.436			
Child–Pugh class	C	257 (71.0%)	1.08	0.74-1.61	0.690			
MELD score	≥20	115 (31.8%)	1.32	0.89-1.93	0.169			
ABO blood type	Incompatible	32 (8.8%)	1.31	0.64-2.39	0.428			
Operative time	≥10 h	148 (40.9%)	1.34	0.93-1.92	0.116	1.33	0.92-1.91	0.124
Blood loss	≥10 l	64 (17.7%)	1.27	0.81-1.94	0.288			
GRWR	≥0.8%	260 (71.8%)	1.00	0.68-1.51	0.981			

CI: Confidence interval; CORE: Cirrhosis Outcome Risk Estimator; GRWR: graft-to-recipient weight ratio; HR: hazard ratio; MELD: Model for End-Stage Liver Disease. Statistically significant p-values are shown in bold.

Table III. *Univariate and multivariate analyses of prognostic factors associated with graft survival after living-donor liver transplantation (n=362).*

			Univariate			Multivariate		
Variable	Subgroup	n (%)	HR	95% CI	*p*-Value	HR	95% CI	*p*-Value
Donor age, years	≥50 years	109 (30.1%)	1.67	1.15-2.40	**0.007**	1.26	0.82-1.94	0.290
Donor sex	Male	197 (54.4%)	1.04	0.73-1.49		0.842		
CORE score	>0.05	196 (54.1%)	1.89	1.31-2.76	**0.001**	1.66	1.07-2.57	**0.024**
Recipient age, years	≥60 years	83 (22.9%)	1.17	0.77-1.74		0.457		
Recipient sex	Male	194 (53.6%)	1.21	0.85-1.74		0.300		
Child–Pugh class	C	257 (71.0%)	1.00	0.69-1.48		0.999		
MELD score	≥20	115 (31.8%)	1.21	0.81-1.77		0.351		
ABO blood type	Incompatible	32 (8.8%)	1.26	0.62-2.29		0.502		
Operative time	≥10 h	148 (40.9%)	1.34	0.94-1.92	0.108	1.33	0.93-1.90	0.120
Blood loss	≥10 l	64 (17.7%)	1.33	0.85-2.00		0.211		
GRWR	≥0.8%	260 (71.8%)	1.14	0.77-1.74		0.534		

CI: Confidence interval; CORE: Cirrhosis Outcome Risk Estimator; GRWR: graft-to-recipient weight ratio; HR: hazard ratio; MELD: Model for End-Stage Liver Disease. Statistically significant p-values are shown in bold.

score was an independent predictor of patient and graft survival after LDLT.

To ensure donor and recipient safety, living donors should be carefully selected based on multiple criteria (13). Graft volume, hepatic steatosis, and donor age are key criteria in the LDLT screening process (14, 15). However, little is known about the evaluation of graft quality using laboratory parameters. Further studies are required to investigate reliable donor prognostic markers associated with prognosis after LDLT.

The CORE score, an easily accessible screening tool, is a newly developed risk model for predicting the 10-year risk of major adverse liver outcomes in the general population (8). In this study, the CORE score assessment was easily adopted for living donors. Owing to the strict selection criteria for living donors, the donor CORE score was low, with a median of 0.07 (Figure 1). Subsequently, the optimal cut-off value of the CORE score was determined to be 0.05 using the Youden index.

In this study, the follow-up period for recipients was sufficiently long to examine the impact of donor CORE scores on long-term outcomes. When stratified by donor CORE score, we observed a significant association between the donor CORE score and recipient outcomes, including patient and graft survival (Figure 2). Moreover, the donor CORE score was an independent predictor of recipient survival after LDLT (Table II and Table III). Although donor laboratory values were normal with a low CORE score, recipient outcomes were significantly stratified using the CORE score. These results suggest that the donor CORE score may be a useful tool for assessing liver graft quality and estimating recipient outcomes. The preoperative assessment of the donor CORE score can be used to determine graft selection.

In the multivariate analyses, other donor and recipient factors were not associated with survival after LDLT. Although a commonly used maximum donor age is 50 years, carefully selected older donors can increase the donor pool (14, 16). The disease severity of recipients, such as the MELD score, especially with concomitant risk factors, has been reported to have the greatest influence on short-term outcomes (17, 18). However, a MELD score ≥20 was not identified as an independent predictor of prognosis in this study. The role of the GRWR has been discussed as a standard selection benchmark for LDLT (19, 20). Our results indicate that a GRWR <0.8% can be used in selected recipients without compromising long-term outcomes.

This study had several limitations. Firstly, this was a retrospective, single-center study with a relatively small sample size, without external validation of the results. Further investigation is required to establish the optimal cut-off value for the donor CORE score. As studies investigating the impact of the CORE score on postoperative outcomes in gastrointestinal surgery are still lacking, the mechanism underlying the association between the CORE score and outcomes remains unknown.

In conclusion, this study demonstrated the clinical significance of the donor CORE score on recipient outcomes after LDLT. The donor CORE score may be useful for estimating the survival of patients undergoing LDLT.

Conflicts of Interest

The Authors declare no conflict of interest regarding this study.

Authors' Contributions

Conception and design: Kosei Takagi. Analysis and interpretation: Kosei Takagi, Tomokazu Fuji, Kazuya Yasui, Takeyoshi Nishiyama, Yasuo Nagai, Naohiro Okada, Shohei Yokoyama. Drafting of the manuscript: Kosei Takagi. Critical revision of the manuscript: Toshiyoshi Fujiwara. All Authors approved the final version of the article.

Artificial Intelligence (AI) Disclosure

No artificial intelligence (AI) tools, including large language models or machine-learning software, were used in the preparation, analysis, or presentation of this manuscript.

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