

Original

Living Donor Liver Transplantation Patients Follow-up : Health-related Quality of Life and Their Relationship with the Donor

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Abstract : Living donor liver transplantation (LDLT) is now an established therapeutic option for end-stage liver disease with overall survival comparable to that following deceased donor liver transplantation. However, the long-term quality of life (QOL) -related issues following LDLT remain to be investigated. In LDLT, the recipient receives an organ from a living donor, often a family member with strong emotional bonds. Unlike in the case of deceased donors, the lasting bond may strongly affect QOL following transplantation. The aims of the present study were to clarify the health-related QOL of LDLT recipients and to evaluate whether live liver donation affects outcomes. Adult LDLT recipients who made regular follow-up outpatient clinic visits to the liver transplantation service at The University of Tokyo Hospital were enrolled in the study. Subjects were surveyed using two self-administered questionnaires, the standard Short Form 36 (SF36) and a self-designed questionnaire addressing social issues specific to LDLT. Over the 3 months of the study, 88 recipients visited the clinic for regular follow-up examinations. Of these, 83 agreed to be interviewed for the study, of whom 72 (87%) provided complete responses. The SF36 scores for physical functioning, role physical (role limitations due to physical health), and social functioning were significantly lower for study participants than for the general Japanese population. A higher level of education and the degree to which the recipient felt indebted to the donor had significant negative effects on SF36 scores. QOL after LDLT may be lower than that of the general population. The continuing emotional bond with live donors after surgery may strongly affect the QOL of adult LDLT recipients.

Key words : difficulties, living donor liver transplantation, quality of life, Short Form 36 (SF36)

Introduction

Liver transplantation is currently accepted as the most effective therapy for end-stage liver disease. Improved surgical techniques and immunosuppressive agents have enhanced the long-term results, leading to an increased demand that exceeds the number of available deceased donor organs. This disparity has reached a critical level in many countries. In Japan, due the limited number of deceased donor organs available, living donor liver transplantation (LDLT) is

performed as a mainstream treatment for end-stage liver disease. The first pediatric case was performed in November 1989 and the first successful adult-to-adult LDLT was performed in 1994¹⁾.

Several studies have focused on health-related quality of life (QOL) after liver transplantation²⁻⁷⁾. The results of these studies suggest that health-related QOL of transplant recipients improves after liver transplantation. The largest gains are observed in the aspects of QOL that involve physical health, whereas fewer gains are observed in areas involving psychological functioning. However, all these studies were conducted with liver transplant recipients who had received a liver from a deceased donor. The issue of health-related QOL in transplant recipients is generating more interest⁸⁾ because LDLT is spreading throughout the world as an effective alternative to deceased donor liver transplantation. Some recent studies have investigated the QOL of LDLT recipients⁹⁻¹³⁾. For example, Urano *et al*⁹⁾ investigated the relationship between nutritional assessment and health-related QOL, Togashi *et al*¹⁰⁾ compared the QOL before and after transplantation, and Kawagishi *et al*¹³⁾ reviewed the long-term outcomes of LDLT in children. However, no study has investigated how the relationship with the donor affects the QOL of LDLT recipients.

In LDLT, the recipient receives an organ from a living donor, often a family member with strong, lasting emotional bonds. Unlike in the case of deceased donors, this lasting bond may strongly affect the QOL following transplantation¹⁴⁾. Whether or not the strong emotional tie between the donor and recipient has a positive or a negative effect on QOL after LDLT remains to be determined. The hypothesis tested in the present study was that the relationship between the recipient and donor, including feelings of appreciation and indebtedness, is correlated with health-related QOL. The present study was conducted to clarify the health-related QOL of LDLT recipients and to evaluate whether live liver donation affects the outcome.

Patients and methods

Adult (≥ 18 years of age) LDLT recipients who made regular follow-up clinic visits over the 3-month study period were eligible for inclusion in the study. The purpose and objectives of the study were explained in detail to each patient during their first clinic visit during the study period, and questionnaires were either handed out or mailed to patients who were willing to participate. In addition to the information obtained from the questionnaires, clinical and social demographics were reviewed retrospectively from medical charts. All procedures in the survey were approved by the Ethics Committee of The University of Tokyo Hospital, and a written consent was obtained from all participants.

Evaluation of health-related QOL after LDLT

To evaluate the health-related QOL of recipients, a validated Japanese version of the Short Form 36 (SF36) was used¹⁵⁾. In the present study, SF36 scores were used as indicators of health-related QOL. The SF36 was developed by Ware and Sherbourne¹⁶⁾. Briefly, the SF36 contains eight subscales, including physical functioning, role physical (role limitations due to physical health), bodily pain, general health, vitality, social functioning, role emotional (role limitations

due to emotional health), and mental health. Each subscale is scored over the range 0–100, with higher scores reflecting better QOL.

Self-designed questionnaire addressing issues specific to LDLT

Pilot interviews were conducted before the study with 20 recipients and 19 donors to develop the questionnaire used in the present study, creating a set of questions focusing on issues involving the live donor. Three questions were designed to evaluate recipients' subjective perceptions and these were rated semiquantitatively using Likert scales:

1. What is your overall general relationship with the donor?
2. To what degree do you appreciate the donor?
3. To what degree do you feel indebted to the donor?

Question 1 was rated on a scale ranging from “far better” to “far worse”, whereas Questions 2 and 3 were rated on a scale ranging from “not at all” to “very much”.

Statistical analysis

Mean SF36 scores for the subjects were compared with those of the general population after adjustment for sex and age¹⁶⁾ using the Wilcoxon signed-rank sum test. To analyze factors associated with SF36 scores, logistic regression analysis was performed using SAS for Windows Version 8.2 (SAS Institute, Cary, NC, USA). The explanatory variables for the analysis included sex, age, length of time after LDLT, medical insurance coverage, level of education, changes in the general relationship with the donor, degree of appreciation of the donor, and degree of feeling indebted to the donor. In all cases, $p < 0.05$ was considered statistically significant.

Results

Demographics

Of a total of 88 liver transplant recipients, 83 were followed as outpatients during the study period. Of the 83 questionnaires delivered, seven were not returned and four were returned with more than 10% incomplete data. Data from the remaining 72 recipients (87%) were analyzed. Of these 72 patients, 33 were men and 39 were women (median age 49 years; range 22–68 years). In 32 cases (44%), the donor was a child of the recipient. The most common indication for LDLT was primary biliary cirrhosis ($n = 19$), followed by hepatitis B virus-related cirrhosis ($n = 17$), hepatitis C virus-related cirrhosis ($n = 13$), and fulminant hepatic failure ($n = 7$). At the time of the survey, 49 patients (68%) had been followed for more than 1 year as an outpatient after LDLT; of these, 13 (18%) had been followed for more than 3 years. Other social factors are summarized in Table 1.

SF36 questionnaire

Compared with the age-matched adjusted Japanese general population, LDLT recipients had a similar QOL with regard to items such as bodily pain, general health, vitality, role emotional, and mental health. The items physical functioning, role physical, and social functioning were

Table 1. Socioeconomic background of study participants

Factors	N (%)
Health insurance coverage	
Yes	47 (65)
No	24 (33)
Level of education	
High school or less	33 (46)
College level or higher	39 (54)

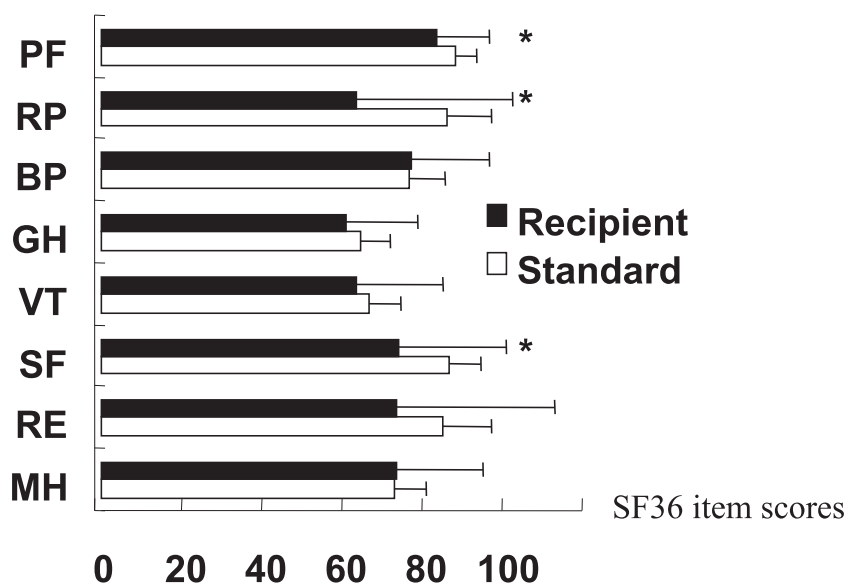


Fig. 1. Short Form 36 (SF36)¹⁵⁾ scores for living donor liver transplantation (LDLT) recipients compared with the adjusted Japanese general population. Data are the mean \pm SD. PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning, RE, role emotional; MH, mental health.

significantly worse in LDLT recipients than in the general Japanese population (Fig. 1).

Self-designed questionnaire

Each recipient's subjective perception of their relationship with the donor was semiquantified using Likert scales (Fig. 2). Only 24% of LDLT recipients felt that the overall general relationship with the donor had improved after LDLT compared with before transplantation. Ninety-two percent expressed a high degree of appreciation of the donor, and 47% felt highly indebted.

Factors associated with SF36 scores

Factors associated with SF36 scores were analyzed by logistic regression analysis (Table 2). Lower physical functioning scores were significantly related to a shorter time period after LDLT ($p=0.04$) and to the degree of feeling indebted to the donor ($p = 0.04$). Lower general health

Respondents rate

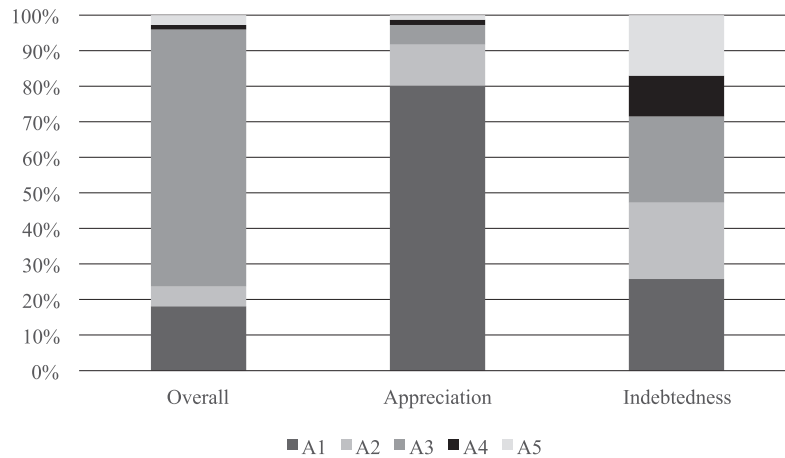


Fig. 2. Recipients' subjective perception of their relationship with the donor, semiquantified using Likert scales. Respondents were asked three questions to determine their relationship with the donor: (1) what is your overall general relationship with the donor; (2) to what degree do you appreciate the donor; and (3) to what degree do you feel indebted to the donor? Perceptions regarding the overall general relationship with the donor compared with the relationship prior to transplantation were rated as far better (A1), better (A2), unchanged (A3), worse (A4), or far worse (A5). The degree of appreciation and the degree of feeling indebted to the donor were rated as very much (A1), considerably (A2), slightly (A3), very little (A4), or not at all (A5).

Table 2. Factors associated with scores for different items on the Short Form 36¹⁵⁾ (SF36)

Variable	PF	RP	BP	GH	VT	SF	RE	MH
Sex	0.59	1.07	1.14	2.67	1.00	1.85	1.55	3.14
Age	0.92	1.24	0.95	0.67	0.95	0.98	0.87	1.54
Days after LDLT	0.59*	0.76	0.81	0.92	0.84	0.75	0.88	0.89
Medical insurance coverage	0.42	1.96	1.94	0.38	0.99	2.13	1.68	1.12
Level of education	0.62	1.30	1.54	6.75*	4.50*	4.24*	0.94	1.22
Changes in the general relationship with the donor	0.82	0.60	0.86	1.00	1.40	1.27	0.95	3.42
Degree of appreciation of the donor	0.24	0.11	< 0.001	2.43	5.95	2.21	0.33	5.26
Degree of feeling indebted to the donor	3.08*	1.39	1.58	4.23*	2.71	1.29	2.46	4.02*

Data show odds ratios. * $p < 0.05$

LDLT, living donor liver transplantation; PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning, RE, role emotional; MH, mental health.

scores were related to the degree of feeling indebted to the donor ($p = 0.03$) and to a higher level of education ($p = 0.004$). Lower vitality and lower social functioning scores were related

to a higher level of education ($p = 0.01$). Low mental health scores were significantly related to the degree of feeling indebted to the donor ($p = 0.02$). Two factors, namely the level of education and the degree to which recipients felt indebted to the donor, had a significant negative effect on SF36 scores.

Discussion

Mean SF36 scores of recipients after LDLT were significantly lower than those of the adjusted general population norms on three subscales, namely physical functioning, role physical, and social functioning. Physical function tended to recover over time after LDLT, although it was not significantly improved in the present small series. These results are compatible with previous studies^{2, 17-20} conducted in deceased donor liver transplantation recipients, who exhibited improvements in physical health aspects but little improvement in mental health-related scores.

Unlike in deceased donor liver transplantation, factor analysis revealed that two factors, namely level of education and the degree to which recipients felt indebted to the donor, had a significant negative effect on QOL in adult LDLT recipients. Poorer physical functioning was related to a shorter length of time after LDLT, but also to a higher degree of feeling indebted to the donor. In living donor renal transplantation, recipients with failed renal grafts feel heavily indebted to the donors who offered them their kidney²¹). This aspect has not been investigated in LDLT. The concern here is that patients who responded in the present study are patients with functioning grafts, which is very different from the published study on patients with failed living related kidney grafts. Having placed a healthy person under the burden of major hepatectomy, and thus being socially obliged to maintain a life-long tie, may be stressful, adding to the feeling of being indebted. This negative emotional drive may affect the QOL of adult LDLT recipients.

Because of the cross-sectional and timing-specific nature of the present study, it was not possible to compare the health status over time of LDLT recipients with that of individuals diagnosed with liver disease who did not receive a liver transplant. Another potential weakness of the present analysis is the possible bias in sample selection. The subjects for the present study were limited to recipients who made regular outpatient clinic visits. Recipients who were rehospitalized for complications during the study period were not included.

Conclusion

QOL after LDLT may be lower than that of the general population. To our knowledge, the present study is the first to investigate how the relationship with the donor affects the QOL of LDLT recipients. An emotional bond with live donors may strongly affect the QOL of adult LDLT recipients. The present study is small and the scope of the socioeconomic and psychosocial factors analyzed was limited. Further studies involving issues related to live donors are necessary.

Conflict of interest disclosure

The author declares that there is no conflict of interest regarding the publication of this article.

References

- 1) Sugawara Y, Makuuchi M. Living donor liver transplantation: present status and recent advances. *Br Med Bull.* 2006;**75-76**:15-28.
- 2) Hellgren A, Berglund B, Gunnarsson U, *et al.* Health-related quality of life after liver transplantation. *Liver Transpl Surg.* 1998;**4**:215-221.
- 3) Bravata DM, Olkin I, Barnato AE, *et al.* Health-related quality of life after liver transplantation: a meta-analysis. *Liver Transpl Surg.* 1999;**5**:318-331.
- 4) Gross CR, Malinchoc M, Kim WR, *et al.* Quality of life before and after liver transplantation for cholestatic liver disease. *Hepatology.* 1999;**29**:356-364.
- 5) Bravata DM, Keeffe EB. Quality of life and employment after liver transplantation. *Liver Transpl.* 2001;**7(11 Suppl 1)**:S119-123.
- 6) Painter P, Krasnoff J, Paul SM, *et al.* Physical activity and health-related quality of life in liver transplant recipients. *Liver Transpl.* 2001;**7**:213-219.
- 7) Ratcliffe J, Longworth L, Young T, *et al.* Assessing health-related quality of life pre- and post-liver transplantation: a prospective multicenter study. *Liver Transpl.* 2002;**8**:263-270.
- 8) Bowling A. The concept of quality of life in relation to health. *Med Sec oli.* 1995;**7**:633-645.
- 9) Urano E, Yamanaka-Okumura H, Teramoto A, *et al.* Pre- and postoperative nutritional assessment and health-related quality of life in recipients of living donor liver transplantation. *Hepatol Res.* 2014;**44**:1102-1109.
- 10) Togashi J, Sugawara Y, Akamatsu N, *et al.* Quality of life after adult living donor liver transplantation: a longitudinal prospective follow-up study. *Hepatol Res.* 2013;**43**:1052-1063.
- 11) Chen PX, Yan LN, Wang WT. Health-related quality of life of 256 recipients after liver transplantation. *World J Gastroenterol.* 2012;**18**:5114-5121.
- 12) Noma S, Hayashi A, Uehara M, *et al.* Comparison between psychosocial long-term outcomes of recipients and donors after adult-to-adult living donor liver transplantation. *Clin Transplant.* 2011;**25**:714-720.
- 13) Kawagishi N, Takeda I, Miyagi S, *et al.* Quality of life and problems affecting recipients more than 10 years after living donor liver transplantation. *Transplant Proc.* 2009;**41**:236-237.
- 14) Surman OS, Cosimi AB, Fukunishi I, *et al.* Some ethical and psychiatric aspects of right-lobe liver transplantation in the United States and Japan. *Psychosomatics.* 2002;**43**:347-353.
- 15) Fukuhara S, Bito S, Green J, *et al.* Translation, adaptation, and validation of the SF-36 Health Survey for use in Japan. *J Clin Epidemiol.* 1998;**51**:1037-1044.
- 16) Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992;**30**:473-483.
- 17) Robinson LR, Switala J, Tarter RE, *et al.* Functional outcome after liver transplantation: a preliminary report. *Arch Phys Med Rehabil.* 1990;**71**:426-427.
- 18) Hunt CM, Tart JS, Dowdy E, *et al.* Effect of orthotopic liver transplantation on employment and health status. *Liver Transpl Surg.* 1996;**2**:148-153.
- 19) Bryan S, Ratcliffe J, Neuberger JM, *et al.* Health-related quality of life following liver transplantation. *Qual Life Res.* 1998;**7**:115-120.
- 20) Aadahl M, Hansen BA, Kirkegaard P, *et al.* Fatigue and physical function after orthotopic liver transplantation. *Liver Transpl.* 2002;**8**:251-259.
- 21) Christensen AJ, Ehlers SL, Raichle KA, *et al.* Predicting change in depression following renal transplantation: effect of patient coping preferences. *Health Psychol.* 2000;**19**:348-353.

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