Increased survival in hepatitis c patients who underwent living donor liver transplant: a case-control study with propensity score matching

Jong Man Kim[1,*], Kwang-Woong Lee[2], Gi-Won Song[3,*], Bo-Hyun Jung[4], Hae Won Lee[5], Nam-Joon Yi[2], Choon Hyuck David Kwon[1], Shin Hwang[3], Kyung-Suk Suh[2], Jae-Won Joh[1], Suk-Koo Lee[1], Sung-Gyu Lee[3]

[1]Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, [2]Department of Surgery, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, [3]Division of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, [4]Department of Surgery, Inje University Haeundae Paik Hospital, Inje University College of Medicine, Busan, [5]Department of Surgery, Seoul Metropolitan Government - Seoul National University Boramae Medical Center, Seoul, Korea

Purpose: There is no consensus regarding the difference in outcomes of HCV in patients who receive living donor liver transplantation (LDLT) or compared to deceased donor liver transplantation (DDLT). The aims of this study were to compare characteristics between LDLT and DDLT groups and to identify risk factors affecting patient survival.
Methods: We retrospectively reviewed the multicenter records of 192 HCV RNA-positive patients who underwent liver transplantation.
Results: Thirty-five patients underwent DDLT, and 146 underwent LDLT. The 1-, 3-, and 5-year patient survival rates were 66.7%, 63.0%, and 63.0% in the DDLT group and 86.1%, 82.3%, and 79.5% in the LDLT group (P = 0.024), respectively. After propensity matching, the patient survival curve of the LDLT group was higher than that of the DDLT group. However, there was no statistically significant difference in patient survival between the 2 groups (P = 0.061). Recipient age ≥ 60 years, LDLT, and use of tacrolimus were positively associated with patient survival in multivariate analyses.
Conclusion: LDLT appears to be suitable for HCV-infected patients if appropriate living donor is available.
[Ann Surg Treat Res 2017;93(6):293-299]

Key Words: Hepatitis C virus, Immunosuppression, Living donors, Tacrolimus, Survival

INTRODUCTION

HCV infection is the most common underlying disease among Western patients requiring liver transplantation (LT). In Korea, 1%–2% of the population is infected with HCV, and 15%–20% of these infected individuals have chronic liver disease related to HCV infection [1]. As HCV prevalence has increased, HCV-related cirrhosis and HCV-related hepatocellular carcinoma (HCC) will gradually become more common indications for LT

in Korea [2].

Recurrent HCV infection after LT is associated with reduced graft and patient survival [3]. Several studies have demonstrated worse survival outcomes in HCV-positive LT patients compared to HCV-negative patients [4]. Recipient, donor, and transplant-related factors are associated with a high risk of severe and progressive HCV disease. Poor donor liver quality, older donor age, prolonged warm and cold ischemia times, donation after cardiac death, and a high donor risk index are associated with

lower graft survival and higher rates of advanced fibrosis [5].

Living donor LT (LDLT) is an important advancement that has expanded the donor pool and decreased wait-list mortality rates [6,7]. Early data have suggested that HCV patients who underwent LDLT had worse outcomes, including increased rates of cholestatic HCV, compared to DDLT recipients [8]. However, recent studies suggest there are no significant differences in outcomes between patients who receive LDLT versus DDLT for HCV-related disease, including graft and patient survival [9-11]. The lack of consensus within the field emphasizes the importance of a better understanding of the optimal mode of LT for HCV-positive patients.

Herein, we compared patient characteristics and survival data of HCV-positive patients who underwent either LDLT or DDLT and identified factors associated with patient survival.

METHODS

Patients

This study was conducted in 3 liver transplantation centers in Korea: Samsung Medical Center (SMC), Asan Medical Center (AMC), and Seoul National University Hospital (SUNH). Because this was a retrospective study, we were not able to request patient consent for the use of clinical records. However, each center's Institutional Review Board (IRB) approved our protocols (Samsung Medical Center IRB No. 2014-07-031, Asan Medical Center IRB No. S2015-1341-0003, Seoul National University Hospital IRB No. 1407-139-597). Present study was exempt from written informed consent at each IRB. We retrospectively evaluated the medical records of patients who underwent their first LT between 1999 and 2012. Data from all consecutive 192 HCV RNA-positive cases during this period were reviewed using the same questionnaire. However, immunosuppression protocols, treatment for organ rejection, and treatment for recurrent HCV infection were not standardized across centers. The laboratory-based model of end-stage liver disease (MELD) score was calculated at the time of transplantation. Information on and/or records of all patients were deidentified prior to analysis. Cases of hospital mortality (n = 11) were excluded from our analysis of risk factor identification. We ultimately investigated risk factors associated with patient survival in 181 patients.

Evaluated variables

The following variables were obtained from our medical record review in response to the survey: patient age, sex, HCV genotype, MELD score, co-occurrence with HCC, coinfection with HBV or HIV, antiviral treatments received after transplantation, type of calcineurin inhibitor received, use of mycophenolate mofetil (MMF), steroid withdrawal, biopsy-proven acute rejection, HCV recurrence, and other outcomes. Additionally, donor age and ischemic time were included as

variables. Finally, we recorded information on patient survival and calculated the time to death. However, we did not incorporate any other incomplete variables that might have been associated with patient survival, such as *IL-28* gene polymorphisms, histological findings, biliary complications, or infectious episodes. Diagnosis of acute rejection was based on internationally accepted histologic criteria (Banff guidelines) using liver biopsies [12]. HCV recurrence was diagnosed based on histology, biochemistry, and/or detection of HCV RNA in the serum.

Propensity score matching

To avoid confounding differences between DDLT and LDLT due to baseline differences between DDLT and LDLT recipients, we performed our analyses with all patients and after propensity score matching. Patients in the DDLT and LDLT groups were matched using propensity scores in IBM SPSS Statistics ver. 21.0 (IBM Co., Armonk, NY, USA). The propensity score of an individual was calculated given the covariates of recipient age, donor age, MELD score, and use of calcineurin inhibitors using a logistic regression model. We applied 1:1 nearest neighbor matching without replacement in order to ensure that conditional bias was minimized. Each patient in the DDLT group was matched to a patient in the LDLT group with the minimum difference in propensity score.

Statistical analyses

Continuous data are reported as the median and range and were compared using the Mann-Whitney U-test. Categorical variables are reported as numeric proportions. Comparisons of categorical data between groups were performed using the chi-square test or Fisher exact test as appropriate. Patient survival rates were evaluated using the Kaplan-Meier method and compared using the log-rank test. Clinical variables found to have prognostic significance by univariate analysis were entered into a Cox multivariate proportional hazards model to determine which factors independently predicted patient survival. The cutoff values for continuous variables were set according to each receiver operating characteristic (ROC) curve. Statistical significance was set at a P-value less than 0.05. Statistical analyses were performed using IBM SPSS Statistics ver. 21.0.

RESULTS

Baseline characteristics

Patient characteristics are shown in Table 1. There were 35 DDLT patients and 146 LDLT patients. Median ages of the DDLT and LDLT recipients were 53 years (range, 34–69) and 57 years (range, 34–72), respectively (P = 0.418); however, the median donor age of the DDLT group was significantly older than that

Table 1. Patient characteristics according to transplant type in all patients

Characteristic	DDLT (n = 35)	LDLT (n = 146)	P-value
Baseline			
Male sex	24 (68.6)	104 (71.2)	0.837
Recipient age ≥60 yr	13 (37.1)	45 (30.8)	0.546
Donor age ≥30 yr	28 (80.0)	78 (53.4)	0.004
HCV genotype			0.617
Unknown	3 (8.6)	8 (5.5)	
Type 1	18 (51.4)	96 (65.8)	
Type 2	12 (34.3)	37 (25.3)	
Type 3	1 (2.9)	3 (2.1)	
Type 6	1 (2.9)	2 (1.4)	
HCV RNA $\geq 1 \times 10^5$ IU/mL	18 (58.1)	74 (50.7)	0.843
MELD score	21 (8–50)	15 (6–40)	0.000
HBV coinfection	4 (11.4)	19 (13.0)	0.800
HCC co-occurrence	11 (31.4)	73 (50.0)	0.059
Perioperative			
Graft type			<0.001
Whole	34 (97.1)	0 (0)	
Right lobe	0 (0)	136 (93.2)	
Left lobe	0 (0)	10 (6.8)	
Split	1 (2.9)	0 (0)	
Cold ischemic time (min)	228 (65–908)	77 (8–1437)	<0.001
Warm ischemic time (min)	44 (20–260)	38 (12–110)	0.124
Posttransplant			
Use of induction (basiliximab)	20 (57.1)	93 (63.7)	0.560
Calcineurin inhibitor use			0.556
None	1 (2.9)	2 (1.4)	
Cyclosporine	16 (45.7)	80 (54.8)	
Tacrolimus	18 (51.4)	64 (43.8)	
Use of MMF	20 (57.1)	91 (62.3)	0.569
Use of steroids (>6 mo)	15 (44.1)	48 (32.9)	0.755
Universal prophylaxis	9 (25.7)	72 (49.3)	0.014
Preemptive treatment	7 (20.0)	8 (5.5)	0.011
Biopsy-proven acute rejection	7 (20.0)	32 (21.9)	0.804
Follow-up (mo)	19 (2–157)	38 (2–151)	0.004

Values are presented as number (%) or median (range).
DDLT, deceased donor liver transplantation; LDLT, living donor liver transplantation; MELD, model of end-stage liver disease; HCC, hepatocellular carcinoma; MMF, mycophenolate mofetil.

of the LDLT group (41 years *vs.* 31 years, P < 0.001). Thus, the proportion of donors in the DDLT group who were older than 30 was 80%, compared to 53.4% in the LDLT group. No significant differences in gender, HCV genotype, HCV RNA, HBV coinfection, or HCC co-occurrence were observed between the 2 groups. The median MELD score of the DDLT group was significantly higher than that of the LDLT group (21 *vs.* 15, P < 0.001).

Perioperative characteristics
Most of the DDLT patients received a whole liver graft (97.1%), while LDLT patients largely received right lobe grafts (91.8%) (P < 0.001). The median graft-to-recipient weight ratio in the LDLT group was 1.08 (range, 0.68–1.20). Warm ischemic time in the DDLT group was not significantly different from that in
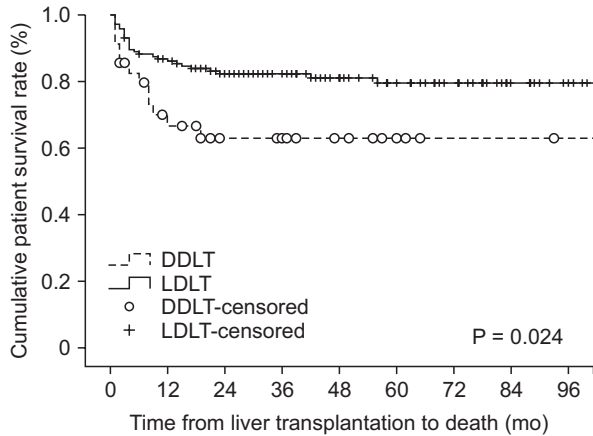
the LDLT group (44 minutes *vs.* 38 minutes, P = 0.124), but cold ischemic time was significantly longer in the DDLT group than in the LDLT group (228 minutes *vs.* 77 minutes, P < 0.001).

Posttransplant characteristics
The median follow-up durations in the DDLT and LDLT groups were 19 months (range, 2–157 months) and 38 months (range, 2–151 months), respectively. There were no statistically significant differences in the use of induction agent, used cyclosporine, used tacrolimus, used MMF, or steroid use for longer than six months, HCV recurrence or biopsy-proven acute rejection between the 2 groups. Most patients in the LDLT group received universal prophylaxis, while most DDLT patients received preemptive treatment.

Patient survival and associated factors

The 1-, 3-, and 5-year patient survival rates were 66.7%, 63.0%, and 63.0%, respectively, in the DDLT group and 86.1%, 82.3%, and 79.5% in the LDLT group (P = 0.024) (Fig. 1). The causes of mortality are summarized in Table 2. Twelve patients in the DDLT group and 28 patients in the LDLT group died during the observation period. The most common cause of death in both groups was sepsis. Univariate analyses revealed that recipient age ≥60 years, LDLT, use of tacrolimus, and biopsy-proven acute rejection were closely associated with increased patient survival. Recipient age ≥60 years, LDLT, and use of tacrolimus were determined to be independent factors associated with

Table 2. Causes of patient mortality

Transplantation	<1 Year	≥1 Year
DDLT (n = 12)	Sepsis (n = 8)	HCV recurrence (n = 1)
	HCV recurrence (n = 2)	
	Chronic rejection (n = 1)	
LDLT (n = 28)	Sepsis (n = 8)	Hepatic failure (n = 2)
	HCC recurrence (n = 3)	Traumatic SDH (n = 1)
	HCV recurrence (n = 4)	Sepsis (n = 2)
	PCP (n = 1)	HCV recurrence (n = 3)
	GI bleeding (n = 1)	
	Chronic rejection (n = 1)	
	Bronchial hemorrhage (n = 1)	
	Cardiomyopathy (n = 1)	

DDLT, deceased donor liver transplantation; LDLT, living donor liver transplantation; HCC, hepatocellular carcinoma; SDH, subdural hemorrhage; PCP, pneumocystitis carinii pneumonia; GI, gastrointestinal.

Fig. 1. Survival curves of all LDLT and DDLT patients. LDLT, living donor liver transplantation; DDLT, deceased donor liver transplantation.

Table 3. Risk factors affecting patient survival

Variable	OR	95% CI	P-value
Univariate			
Male sex	0.751	0.367–1.538	0.434
Recipient age ≥60 years	2.311	1.233–4.331	0.009
HCV RNA ≥1×10^5	0.779	0.390–1.559	0.481
HBV coinfection	0.736	0.262–2.070	0.561
HCC co-occurrence	1.016	0.545–1.894	0.959
MELD	1.012	0.975–1.051	0.533
Donor type (LDLT)	0.469	0.238–0.924	0.029
Donor age ≥30 years	1.833	0.912–3.683	0.089
Cold ischemic time (minutes)	1.000	0.998–1.002	0.813
Induction immunosuppression (basiliximab)	0.771	0.409–1.454	0.771
Use of tacrolimus	0.455	0.231–0.897	0.023
Use of MMF	0.787	0.420–1.475	0.454
Universal prophylaxis	1.361	0.726–2.550	0.337
Preemptive treatment	0.484	0.115–2.036	0.322
HCV recurrence	0.881	0.467–1.660	0.695
Biopsy-proven acute rejection	2.099	1.095–4.024	0.026
Multivariate			
Recipient age ≥60 years	2.379	1.266–4.469	0.007
Donor type (LDLT)	0.456	0.230–0.902	0.024
Use of tacrolimus	0.406	0.205–0.802	0.009

OR, odds ratio; CI, confidence interval; HCC, hepatocellular carcinoma; MELD, model of end-stage liver disease; LDLT, living donor liver transplantation; MMF, mycophenolate mofetil.

patient survival in multivariate analyses (Table 3).

Characteristics after propensity score matching

Propensity score matching analysis created 31 pairs of patients. Baseline, perioperative, and post-transplant characteristics except cold ischemic time and graft type were similar between the two matched groups (Table 4). The cold ischemic time in the DDLT group was longer than that in the LDLT group (P < 0.001). After propensity matching, the patient survival curve of the LDLT group was higher than that of the DDLT group. The 1-year patient survival rates of the DDLT and LDLT groups were 62.7% and 87.1%, respectively (P = 0.024). However, there was no statistically significant difference in patient survival curve between the 2 groups (P = 0.061) (Fig. 2).

DISCUSSION

In this multicenter study, we found that HCV RNA-positive patients who underwent LDLT had significantly higher survival rates than patients who underwent DDLT. However, DDLT recipients had worse prognostic factors, such as older donor age, higher MELD score, and longer cold ischemic time, compared with LDLT recipients.

A previous study reported a worse graft outcome and more aggressive recurrent hepatitis C after LDLT compared with DDLT because of genetic similarity between the donor and recipient and enhanced HCV replication by intense hepatocyte proliferation in partial liver grafts [8]. The worse outcomes reported after LDLT might have been due to an increased rate of

Table 4. Patient characteristics according to transplant type after propensity matching

Characteristic	DDLT (n = 31)	LDLT (n = 31)	P-value
Baseline			
Male sex	21 (67.7)	21 (67.7)	1.000
Recipient age ≥60 yr	13 (41.9)	6 (19.4)	0.097
Donor age ≥30 yr	25 (80.6)	22 (71.0)	0.554
HCV genotype			0.824
Unknown	2 (6.5)	3 (9.7)	
Type 1	16 (51.6)	18 (58.1)	
Type 2	11 (35.5)	9 (29.0)	
Type 3	1 (3.2)	1 (3.2)	
Type 6	1 (3.2)	0 (0)	
HCV RNA ≥1 × 10^5 IU/mL	17 (60.7)	11 (37.9)	0.114
MELD	20 (8–38)	20 (11–40)	0.961
HBV coinfection	3 (9.7)	1 (3.2)	0.612
HCC co-occurrence	11 (35.5)	10 (32.3)	0.788
Perioperative			
Graft type			<0.001
Whole	30 (96.8)	0 (0)	
Right lobe	0 (0)	30 (96.8)	
Left lobe	0 (0)	1 (3.2)	
Split	1 (3.2)	0 (0)	
Cold ischemic time (min)	224 (65–463)	78 (27–223)	<0.001
Warm ischemic time (min)	44 (20–260)	37 (12–87)	0.093
Posttransplant			
Use of induction (basiliximab)	17 (54.8)	23 (74.2)	0.184
Calcineurin inhibitor			0.833
None	1 (3.2)	2 (6.5)	
Cyclosporin	14 (45.2)	14 (45.2)	
Tacrolimus	16 (51.6)	15 (48.4)	
Use of MMF	17 (54.8)	22 (71.0)	0.293
Use of steroids (>6 mo)	14 (46.7)	10 (32.3)	0.543
Universal prophylaxis	9 (29.0)	9 (29.0)	1.000
Preemptive treatment	6 (19.4)	2 (6.5)	0.255
Biopsy-proven acute rejection	6 (19.4)	11 (35.5)	0.251
Follow-up (mo)	18 (2–157)	36 (2–96)	0.048

Values are presented as number (%) or median (range).
DDLT, deceased donor liver transplantation; LDLT, living donor liver transplantation; MELD, model of end-stage liver disease; HCC, hepatocellular carcinoma; MMF, mycophenolate mofetil.

ASTR
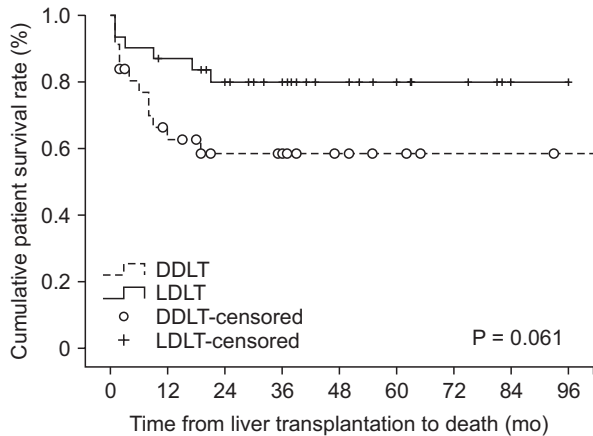
Fig. 2. Survival curves of propensity-matched LDLT and DDLT patients. LDLT, living donor liver transplantation; DDLT, deceased donor liver transplantation.

biliary complications or other problems experienced during the learning-curve years of LDLT [13,14]. Among the 3 centers that participated in this study, more than 100 LDLTs are performed annually.

More recent studies have reported improved results in LDLT recipients compared with DDLT because of the young age of the living donor and shorter ischemic time of LDLT [15]. Generally, DDLT recipients have a higher MELD score than LDLT recipients. High MELD score is considered an independent prognostic factor for severe recurrent HCV and worse patient or graft outcome; therefore, the above data should be evaluated with caution [16]. Similar outcomes were observed for LDLT and DDLT in a recent study using adjusted MELD scores and donor age [15].

Patient enrolled in the present study had similar baseline characteristics compared with those in previous studies. Donor age was younger and cold ischemic time was shorter in the LDLT group than in the DDLT group. However, donor age was not significantly associated with recipient survival in our study, most likely because the median donor age in the present study was young (32 years old) due to the higher proportion of LDLT cases. However, the Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL) found no statistical difference in the 5-year cumulative risk of advanced fibrosis between LDLT and DDLT patients (44% in LDLT patients *vs.* 37% in DDLT patients, P = 0.16) [13]. In addition, they reported that the 5-year unadjusted patient and graft survival probability were 79% and 78% in LDLT and 77% and 75% in DDLT, respectively [13]. The present study showed that the 5-year unadjusted patient survival rate was 63% in DDLT and 79.5% in LDLT. In the A2ALL study, the median MELD score in the DDLT group was 19 points (range, 14–25), whereas that in the present study was 20 points (range, 8–38). Median MELD score was similar between present study and A2ALL study, but the

range of MELD scores in the present study was wider than in the A2ALL study.

LDLT offers a survival advantage for wait-listed patients compared to DDLT [17]. With an increasing number of patients in need of organs, LDLT is an important means of expanding the donor pool. LDLT has several advantages over DDLT, including a shorter waiting time, lower dropout rate, reduced cold ischemia time, and a more thorough pretransplant evaluation for both the donors and recipients. However, most single-center studies have suggested that HCV disease severity among LDLT recipients is either similar or worse than that among DDLT patients [9]. We compared LDLT and DDLT patients using propensity score matching because of differences in baseline characteristics such as recipient age, donor age, MELD score, and calcineurin inhibitors. Cold ischemic time was not matched, however, due to the large difference between the DDLT and LDLT groups. After matching, the patient survival curve of the LDLT group was better than that of the DDLT group. However, the survival difference between the 2 groups was not statistically significant; only the 1-year patient survival rate in the LDLT group was higher than that in the DDLT group (87.1% *vs.* 62.7%; P = 0.024). Long ischemic time is related to ischemic-reperfusion injury, which contributes to increased morbidity and mortality after LT [18]. The present study showed that long cold ischemic time in DDLT recipients resulted in worse patient survival than LDLT recipients despite matching of important variables.

In our study, HCV-infected patients were treated with a combination of interferon and ribavirin. Since the introduction of direct-acting antivirals (DAA) in 2011, sustained viral response 12 weeks after treatment can be achieved in 70% of recurrent HCV liver recipients [19]. Sofosbuvir-based therapy is recommended in the pre- and posttransplant periods [20]. In this era of DAA, there are not likely to be differences in the outcomes of DDLT and LDLT HCV-infected recipients.

There are several limitations inherent to the study design, including variability in documentation, differences in selection criteria and data collection, and missing data. The present study was also seriously weakened by the imbalance in the number of subjects between the 2 groups. To minimize variability, we sent a standardized collection form containing 56 questions to each participating transplant center. Answers were either multiple-choice or involved providing a name or a specific value. However, the quality of the pretransplant interviews from which the baseline data were derived and the quality of the posttransplant follow-up data across the three centers were variable. In addition, the present study did not have a uniform policy for antiviral therapy in HCV recurrence after LT because of its multicenter nature. Furthermore, subjects had varying follow-up durations. We also did not have data on the onset of biopsy-proven acute rejection or the date of graft

failure. Additionally, a lack of data regarding the interleukin-28B genotype of donors and recipients and the presence of fibrosis on biopsy are important limitations of this study. We used propensity score matching to minimize the influence of differences in baseline characteristics; however, given the small number of cases evaluated in the present study, the results should be interpreted with caution. To address these limitations, a well-designed prospective study is needed.

In conclusion, we showed that the survival of patients who underwent LDLT was higher than that of patients who underwent DDLT when the DDLT recipients had poor prognostic factors. Survival rates of LDLT recipients were similar to those of DDLT recipients after propensity score matching. Thus, LDLT appears to be suitable for HCV-infected patients if an appropriate living donor is available in this era of DAA.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Shon HS, Choi HY, Kim JR, Ryu SY, Lee YJ, Lee MJ, et al. Comparison and analysis of the prevalence of hepatitis C virus infection by region in the Republic of Korea during 2005-2012. Clin Mol Hepatol 2015;21:249-56.

2. Kim JM, Lee KW, Song GW, Jung BH, Lee HW, Yi NJ, et al. Outcomes for patients with HCV after liver transplantation in Korea: a multicenter study. Ann Surg Treat Res 2016;90:36-42.

3. Howell J, Angus P, Gow P. Hepatitis C recurrence: the Achilles heel of liver transplantation. Transpl Infect Dis 2014;16:1-16.

4. Lake JR, Shorr JS, Steffen BJ, Chu AH, Gordon RD, Wiesner RH. Differential effects of donor age in liver transplant recipients infected with hepatitis B, hepatitis C and without viral hepatitis. Am J Transplant 2005;5:549-57.

5. Berenguer M, Schuppan D. Progression of liver fibrosis in post-transplant hepatitis C: mechanisms, assessment and treatment. J Hepatol 2013;58:1028-41.

6. Lee SG. A complete treatment of adult living donor liver transplantation: a review of surgical technique and current challenges to expand indication of patients. Am J Transplant 2015;15:17-38.

7. Olthoff KM, Smith AR, Abecassis M, Baker T, Emond JC, Berg CL, et al. Defining long-term outcomes with living donor liver transplantation in North America. Ann Surg 2015;262:465-75.

8. Garcia-Retortillo M, Forns X, Llovet JM, Navasa M, Feliu A, Massaguer A, et al. Hepatitis C recurrence is more severe after living donor compared to cadaveric liver transplantation. Hepatology 2004;40:699-707.

9. Hu A, Liang W, Zheng Z, Guo Z, He X. Living donor vs. deceased donor liver transplantation for patients with hepatitis C virus-related diseases. J Hepatol 2012;57:1228-43.

10. Mitchell O, Gurakar A. Management of hepatitis C post-liver transplantation: a comprehensive review. J Clin Transl Hepatol 2015;3:140-8.

11. Terrault NA, Shiffman ML, Lok AS, Saab S, Tong L, Brown RS Jr, et al. Outcomes in hepatitis C virus-infected recipients of living donor vs. deceased donor liver transplantation. Liver Transpl 2007;13:122-9.

12. Banff Working Group on Liver Allograft Pathology. Importance of liver biopsy findings in immunosuppression management: biopsy monitoring and working criteria for patients with operational tolerance. Liver Transpl 2012;18:1154-70.

13. Terrault NA, Stravitz RT, Lok AS, Everson GT, Brown RS Jr, Kulik LM, et al. Hepatitis C disease severity in living versus deceased donor liver transplant recipients: an extended observation study. Hepatology 2014;59:1311-9.

14. Brown RS Jr. Living donor liver transplantation for HCV: will the true outcomes stand up? J Hepatol 2012;57:1166-7.

15. Jain A, Singhal A, Kashyap R, Safadjou S, Ryan CK, Orloff MS. Comparative analysis of hepatitis C recurrence and fibrosis progression between deceased-donor and living-donor liver transplantation: 8-year longitudinal follow-up. Transplantation 2011;92:453-60.

16. Akamatsu N, Sugawara Y. Liver transplantation and hepatitis C. Int J Hepatol 2012;2012:686135.

17. Berg CL, Merion RM, Shearon TH, Olthoff KM, Brown RS Jr, Baker TB, et al. Liver transplant recipient survival benefit with living donation in the model for endstage liver disease allocation era. Hepatology 2011;54:1313-21.

18. Grassi A, Ballardini G. Post-liver transplant hepatitis C virus recurrence: an unresolved thorny problem. World J Gastroenterol 2014;20:11095-115.

19. Charlton M, Gane E, Manns MP, Brown RS Jr, Curry MP, Kwo PY, et al. Sofosbuvir and ribavirin for treatment of compensated recurrent hepatitis C virus infection after liver transplantation. Gastroenterology 2015;148:108-17.

20. Korean Association for the Study of the Liver. KASL clinical practice guidelines: management of chronic hepatitis B. Clin Mol Hepatol 2016;22:18-75.