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Impact of educational levels on survival rate

A cohort study of 2007 living donor liver transplant recipients at a single large center

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Abstract

Among living donor liver transplantation recipients, the impact of educational levels on survival has rarely explored. Thus, the purpose of study is to analyze the survival rate differences across educational levels among recipients who underwent living donor liver transplantation.

We retrospectively analyzed 2007 adult recipients who underwent living donor liver transplantation in a single large center. The educational level was divided into three categories: middle school or lower, high school, and college or higher. The primary outcome was all-cause mortality after living donor liver transplantation. Stratified log-rank test and Cox proportional hazard model were employed for statistical analysis.

The incidence rates of all-cause mortality were 23.85, 20.19, and 18.75 per 1000 person-year in recipients with middle school or lower, high school, and college or higher education groups, respectively. However, the gender-stratified log-rank test has not shown a statistically significant difference ($P = .3107$). In the unadjusted model, hazard ratio (HR) was 1.02 [95% confidence interval (CI) = 0.79–1.33] in high school and 1.23 (95% CI = 0.93–1.64) and in middle school or lower educational level, respectively; In the full adjusted model, the HR of high school was 0.98 (95% CI = 0.75–1.28) and the HR of middle school or lower was 1.01 (95% CI = 0.74–1.37).

Although study population of this study is large, we could not find significant survival rate differences by the levels of education. Social selection and high compliance rate might contribute to this result.

Abbreviations: ARDS = acute respiratory distress syndrome, BMI = body mass index, CI = confidence interval, ESLD = end-stage liver disease, HCC = hepatocellular carcinoma, HR = hazard ratio, LDLT = living donor liver transplantation, MELD = model for end-stage liver disease, PY = person-year, SES = socioeconomic status.

Keywords: education, living donor liver transplantation, socioeconomic status, survival

1. Introduction

Currently, liver transplantation is the only curative method for end-stage liver disease (ESLD). Majority liver transplantations performed in Korea are living donor liver transplantations (LDLT) owing to the shortage of deceased donors. Recipient survival after LDLT has improved, since 1994 when the first LDLT was performed in Korea. After 2010, the 5-year survival rate of the large liver transplantation center in Korea have reached approximately 90%.[1] Similarly, large transplantation centers in the United States have reported favorable results on recipient survival.[2,3]

Health inequality among different socioeconomic status (SES) is a widespread social concern.[4] Heath inequality is observed in most health outcomes, including average life expectancy and mortality, cardiovascular disease, and cancers.[4–6] Several previous studies on survival of liver transplantation recipients explored survival among patients from different ethnic groups and neighborhood socioeconomic status. As observed in health equality among general populations, previous research reported that survivals of recipients with low SES tended to have a poor prognosis after liver transplantation.[7,8]

Education is an important determinant of health. Educational levels are related to young ages' socioeconomic status; educational levels can influence future occupations and adulthood income which are linked to available material resources which are required to maintain health. Furthermore, education levels can be more important, particularly, among transplant recipients because educational levels can affect health literacy and compliance rate. Compliance rate and health literacy could influence the survival of recipients because maintenance of immunosuppressive regimens and regular visits to outpatient clinics are vital for good prognosis after transplantation.[9–13]

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Compared to deceased donor liver transplantation, LDLT recipients are expected to have more supportive family or social circumstances because living donor liver transplantations are required living donors who have to bear the burden of donation operation. Their supportive family relationship or social circumstance could positively affect the prognosis. However, few studies investigate survival differences, linked with socioeconomic status particularly among LDLT recipients. Therefore, the aim of study is to investigate the survival rate difference of LDLT recipients across different educational levels in a single large center cohort.

2. Methods

2.1. Study population

Between January 2004 and December 2011, we evaluated all 2010 adult recipients who underwent LDLT at a single large liver transplantation center. Of these, three recipients were excluded from analyses because there was no available information about their educational levels. Therefore, the final analysis was conducted in 2007 LDLT recipients. We retrospectively analyzed their electronic medical records. The study protocol was approved by the Asan Medical Center Institutional Review Board (approval number 2015-0589).

2.2. Outcome variables and covariates

All-cause mortality was the primary outcome of this study. Causes of mortality are described in the results. Mortality cases were followed up until December of 2016. This allowed a minimum follow-up of 5 years. The primary explanatory variable was the educational level. The educational level was divided into three categories: middle school or lower, high school, and college or higher. Covariates included age, gender, body mass index, etiologies of liver transplantation, the preoperative model for end-stage liver disease (MELD) scores, smoking habits, alcohol consumption, hypertension, and diabetes.

2.3. Statistical analysis

Comparisons of continuous variables were tested with ANOVA, and the association of categorical variables was tested by Chi-square or Fisher's exact test, as appropriate. The incidence rate was calculated as incidence divided by person-years (PY). The survival curve was drawn by Kaplan–Meier survival estimates, and to test the equality of survivor functions gender-stratified log-rank tests were conducted. For multivariable survival analysis, we employed a Cox Proportional Hazard model. To test the proportionality assumption, Schoenfeld's partial residuals were used. The statistically significant level was $P < .05$. All statistical analyses were performed using Stata Version 13.1 (Stata Corp, College Station, TX).

3. Results

3.1. Characteristics of the study population

Characteristics of the study population are shown in Table 1. The average age of the study population was 50.68 ± 8.34 years, and

Table 1

Characteristics of the study population.

	Middle school or lower (n = 495)	High school (n = 793)	College or higher (n = 719)	*P*
Age, years	54.3 ± 6.2	49.8 ± 8.5	49.1 ± 8.7	<.001
Gender				<.001
Male	281 (56.8)	594 (75.0)	622 (86.5)	
Female	214 (43.2)	199 (25.1)	97 (13.5)	
BMI, kg/m^2	24.1 ± 3.5	24.2 ± 3.4	24.1 ± 6.9	.871
MELD score	17.9 ± 9.0	18.6 ± 9.7	17.8 ± 9.5	.231
Marital status				.001
Unmarried	6 (1.2)	33 (4.2)	40 (5.6)	
Married	478 (96.6)	742 (93.6)	673 (93.6)	
Divorced, widowed, etc.	11 (2.2)	18 (2.3)	6 (0.8)	
Smoking				<.001
None	323 (65.3)	410 (51.7)	383 (53.3)	
Ex-smoker	148 (29.9)	307 (38.7)	297 (41.3)	
Current-smoker	24 (4.9)	76 (9.6)	39 (5.4)	
Alcohol consumption				.001
None	296 (59.8)	408 (51.5)	387 (53.8)	
Social	122 (24.7)	246 (31.0)	243 (33.8)	
Heavy	77 (15.6)	139 (17.5)	89 (12.4)	
Hypertension				.138
No	434 (87.7)	718 (90.5)	654 (91.0)	
Yes	61 (12.3)	75 (9.5)	65 (9.0)	
Diabetes				.348
No	389 (78.6)	622 (78.4)	584 (81.2)	
Yes	106 (21.4)	171 (21.6)	135 (18.8)	
Causes of liver transplantation				<.001
Viral	384 (77.6)	586 (73.9)	603 (83.9)	
Alcohol	43 (8.7)	86 (10.8)	41 (5.7)	
Fulminant	21 (4.2)	50 (6.3)	39 (5.4)	
Others	47 (9.5)	71 (9.0)	36 (5.0)	

Data are expressed as mean ± SD or number (%) of living donor liver transplant recipients as appropriate.
BMI = body mass index, MELD = model for end-stage liver disease.

Table 2

Incidence rate of death based on the educational level.

	Educational level				
	Middle school or lower	High school	College or higher	Total	*P*
Both gender recipients					.311
Person-year	3648.13	5845.84	5599.30	15093.27	
Death	87	118	105	310	
Rate (95% CI)*	23.85 (19.33–29.42)	20.19 (16.85–24.18)	18.75 (15.49–22.71)	20.54 (18.38–22.96)	
Male recipients					.394
Person-year	2024.79	4315.46	4894.37	11234.62	
Death	49	92	88	229	
Rate (95% CI)*	24.20 (18.29–32.02)	24.32 (17.38–26.15)	17.98 (14.59–22.16)	20.38 (17.91–23.20)	
Female recipients					.352
Person-year	1623.34	1530.38	704.93	3858.65	
Death	38	26	17	81	
Rate (95% CI)*	23.41 (17.03–32.17)	16.99 (11.56–24.95)	24.12 (14.99–38.79)	20.99 (16.88–26.10)	

* Rate: death/1000 person × year.
CI = confidence interval.

average preoperative MELD score was 18.15 ± 9.45. With respect to the marital status, recipients with middle school or lower educational levels were more often married (96.57%, $P = .001$). The highest proportion of current smokers was among those with high school educational levels (9.58%, $P < .001$). Similarly, the proportion of recipients with heavy alcohol consumption was the highest among high school graduates (17.53%, $P = .001$). Etiologies of liver transplantation are also shown in Table 1. Approximately 78% of LDLT were because of ESLD caused by chronic viral hepatitis (hepatitis B and C). Recipients with college or higher educational levels exhibited the highest proportion of chronic viral hepatitis as the etiology of liver transplantation (83.87%, $P < .001$).

3.2. Incidence rate of death and survival curve

The total incidence rate was 20.54 per 1000 PY [95% confidence interval (CI) 18.38–22.96], as seen in Table 2. The incidence rate in both genders was the highest in recipients with middle school or lower educational levels [23.85/1000 PY (95% CI 19.33–29.42)] and the lowest in those with college or higher educational levels [18.75/1000 PY (95% CI 15.49–22.71)].

Survival curve of LDLT recipients with 3 different educational levels was demonstrated in Figure 1. The equality of survivor functions was assessed by gender-stratified log-rank test and there were no statistically significant differences in neither male ($P = .3938$) nor female recipients ($P = .352$).

3.3. Causes of death

As shown in Table 3, the most common cause of death was cancer recurrence or metastasis (33.23%) followed by sepsis (23.87%). In recipients with middle school or lower educational levels, the percentage of deaths due to pneumonia or acute respiratory distress syndrome was higher than that observed in those with higher educational levels. In addition, the percentage of those

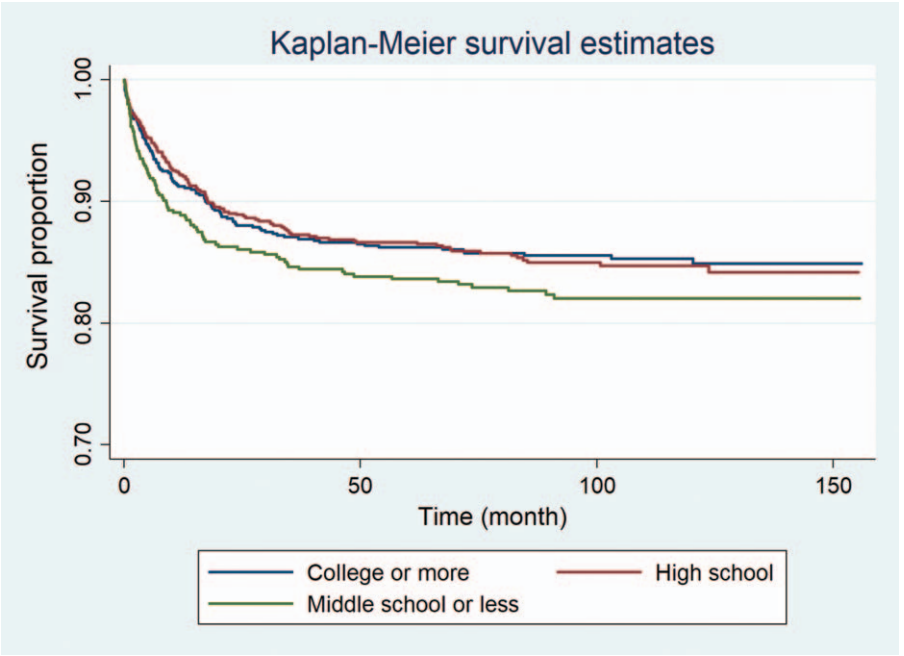

Figure 1. Survival curves of Kaplan–Meier survival estimates in living donor liver transplantation recipients with different educational levels.

Table 3

Causes of death by educational level.

	Middle school or lower	High school	College or higher	Total
Recurrent HCC or cancer metastasis	21 (24.1)	42 (35.6)	40 (38.1)	103 (33.2)
Sepsis	21 (24.1)	24 (20.3)	29 (27.6)	74 (23.9)
Pneumonia or ARDS	15 (17.2)	17 (14.4)	9 (8.6)	41 (13.2)
Graft failure	8 (9.2)	8 (6.8)	6 (5.7)	22 (7.1)
Cardiac and cerebrovascular	7 (8.1)	6 (5.1)	7 (6.7)	20 (6.5)
Rejection	6 (6.9)	2 (1.7)	3 (2.9)	11 (3.6)
Bleeding	1 (1.1)	2 (1.7)	4 (3.8)	7 (2.3)
Others	5 (5.8)	10 (8.5)	6 (5.7)	21 (6.8)
Unknown	3 (3.5)	7 (5.9)	1 (1.0)	11 (3.6)
Total	87 (100.00)	118 (100.00)	105 (100.00)	310 (100.00)

Data are expressed as number (%).

ARDS = acute respiratory distress syndrome, HCC = hepatocellular carcinoma.

who died because of graft failure (9.2%) or rejection (6.9%) was higher among recipients with middle school or lower educational levels. However, this difference was not statistically significant ($P = .263$).

3.4. Hazard ratios (HRs) across educational levels

When other covariates were not adjusted, HRs for all-cause mortality were 1.02 (95% CI: 0.79–1.33) and 1.23 (95% CI: 0.93–1.64) in recipients with high school and middle school or lower educational levels, respectively, compared with those in recipients with college or higher educational levels (Table 4). However, this was not statistically significant. When age, gender, smoking, alcohol, marital status, hypertension, diabetes, and health insurance status were adjusted (model 1 in Table 4), HR of recipients with high school educational levels was 1.00 (95% CI 0.76–1.30), and HR of those with middle school or lower educational levels was 1.02 (95% CI 0.75–1.38). When age, gender, smoking, alcohol, marital status, hypertension, diabetes and health insurance status, etiologies of liver transplantation, and preoperative MELD scores were adjusted (model 2 in Table 4), HR of recipients with high school educational levels was 0.98 (95% CI 0.75–1.28), and HR of those with middle school or lower educational levels was 1.01 (95% CI 0.74–1.37). After these adjustments, we did not observe significant differences among the groups. The proportionality assumption was tested using Schoenfeld's partial residuals. No models violated the proportionality assumption (P values of the unadjusted model, model 1, and model 2 were 0.3077, 0.5672, and 0.2959, respectively).

4. Discussion

To the best knowledge of authors, this study might be the first study to explore the survival of patients who consisted of only LDLT recipients across different educational levels. The previous studies included recipients from both deceased donor and LDLT. Although we could not conduct a noninferiority test, this study has sufficient statistical power to detect the difference, because this study had a large sample size and long-term follow-up period (more than 5 years). In this study, lower educational levels of recipients had a slightly poor prognosis. However, statistically significant survival differences across the different educational levels were not observed in both the unadjusted model and the adjusted model. This result might imply that significant health inequality might not be observed among some specific subpopulations in Korean.

The educational level is an important determinant of health status. Many studies reported that the educational level was consistently associated with all-cause mortality and the incidence of cardiovascular disease and mental health problems, particularly in the general population.[14–17] In general, the educational level could enhance opportunities for better jobs and future income. Also, the educational level is linked with cognitive function could, therefore, influence health-related decision making, including health behaviors and compliance.[18–20] In contrast to previous studies, the educational level did not significantly affect the survival rate among recipients of living donor liver transplantation.

Previous studies explored health inequality among liver transplantation recipients. Several studies showed different prognosis among different educational levels. A study conducted in the United States on survival after liver transplantation reported a slight survival difference by the educational level of recipients. Compared to bachelor degrees, the HR of high school graduate was 1.19 (95% CI 1.04–1.35) in 5-year survival.[8] Similarly, a study from Italy compared different survival rates between patients with lower and higher educational levels. The study showed that recipients with higher educational level had a

Table 4

Hazard ratios based on the educational level using the Cox proportional hazard model.

	Unadjusted		Model 1		Model 2	
Education	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
College or higher	Reference		Reference		Reference	
High school	1.02 (0.79–1.33)	.871	1.00 (0.76–1.30)	.971	0.98 (0.75–1.28)	.867
Middle school or lower	1.23 (0.93–1.64)	.147	1.02 (0.75–1.38)	.917	1.01 (0.74–1.37)	.966

Hazard ratios of model 1 for all-cause mortality are adjusted by age, gender, smoking, alcohol, marital status, hypertension, diabetes, and health insurance status. Hazard ratios of model 2 for all-cause mortality are adjusted by MEDL scores and causes of liver transplantation in addition to all covariates of model 1.

CI = confidence interval, HR = hazard ratio, MEDL = model for end-stage liver disease.

better prognosis and the adjusted HR of higher education was 0.68 (95% CI: 0.21–2.15).[21] Apart from the educational level, recipient ethnicity may affect survival rate. Generally, white recipients have a better prognosis after liver transplantation.[7,22,23]

Unexpectedly, we could not find significant prognosis gap across different educational levels among LDLT recipients. Inconsistency between previous studies and present study might be explained by selections. Selection process might be consist of 2 phases. The first phase might be the social selection (better economic status and social relationship); the second phase of selection is patient selection process at the hospital. Most of the patients have to have consultations with medical staffs before transplantation operations. Through this process, patients who are expected to high compliance can be candidates of liver transplantation.

LDLT recipients tend to be in favorable social environmental, regardless of their educational level, particularly financial status and social relationship. Recipients who undergo liver transplantation might be financially stable regardless of educational background. In Korea, a significant proportion of medical cost paid from out of patients' pocket, because Korean health insurance has not fully covered the medical cost. In this situation, among chronic liver disease patient, persons who could afford to pay the medical cost, tend to be recipients of liver transplantation. Furthermore, LDLT recipients are expected to have supportive family or social circumstances. Although mortality rate of liver donation operation is extremely low, few people would donate their own liver in the absence of supportive relationships with the recipient. Previous studies report that supportive social relationships and marital status were related with better prognosis in hematopoietic stem cell transplantation and orthotopic heart transplantation.[24,25] These 2 social conditions might partially contribute to similar survival rates across different educational levels.

The high compliance of the study population may be another considerable point of the present study. Compliance is vital for recipient survival. Adherence with immunosuppressive agents and regular outpatient visits is very important for better prognosis.[9–11] Prudent recipient selection processes before transplantation and well-organized educational programs for recipients might improve the compliance of recipients in this study, regardless of their educational background. As reported in Table 3, the low proportion of graft failures (7.1%) and rejections (3.6%) reflected the high compliance rate of this study population.

Nevertheless, the result of this study cannot be extended to whole patients with chronic liver disease, because the population of this study is very highly selective and site specific. The population of this study is likely in socio-economically favorable circumstances than patients who could not undergo liver transplantation. Some studies reported health inequalities among patients with chronic liver disease.[26,27] To investigate health inequalities, long-term survival and quality of life of all patients with chronic liver diseases, including those who could not have the opportunity to undergo liver transplantation, should be explored in future studies. Finally, this study was conducted at one of the largest LDLT centers in the world. This team has performed more than 3000 cases of total liver transplantation and annually more than 300 LDLT since 2010.[28] Thus, the results from the present study may differ from those of studies performed at other institutions or from those of multicenter studies.

5. Conclusions

In the present study, we could not find the survival difference among LDLT recipients across different educational levels. This result may be explained by social selection and high compliance rate. We believed that health inequality among recipient of liver transplantation could be attenuated under the supportive social environment and by the high compliance to medical treatment.

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