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 ($P=0.3107$). 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 transplantsions 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]
Compared to deceased donor liver transplantation, LDLT recipients are expected to have more supportive family or social circumstances because living donor liver transplants 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/m² | 24.1 ± 3.5 | 24.2 ± 3.4 | 24.1 ± 3.9 | .871 |
| MELD score | 17.9 ± 9.0 | 18.6 ± 9.7 | 17.9 ± 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 (60.8) | 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 (73.0) | 603 (83.9) |  |
| Alcohol | 43 (8.7) | 86 (10.4) | 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.
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](https://example.com/figure1.png)

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

| Educational level | Middle school or lower | High school | College or higher | Total |
|-------------------|------------------------|------------|------------------|-------|
| Person-year       | 3648.13                | 5845.84    | 5509.30          | 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) |

**Table 2**

Incidence rate of death based on the educational level.

*Rate: death/1000 person \( \times \) year. CI = confidence interval.
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 sub-populations 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. 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.

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. 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 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.

### Table 4

| Education               | Hazard Ratios Unadjusted | HR (95% CI) | P     | HR (95% CI) | P     | HR (95% CI) | P     |
|-------------------------|--------------------------|-------------|-------|-------------|-------|-------------|-------|
|                         |                          | Unadjusted  | Model 1 | Model 2     |       | Model 2     |       |
| Education               | HR (95% CI)              | P          |       |             |       |             |       |
| College or higher       | Reference                | Reference  | Reference | Reference |       | Reference |       |
| High school             | 1.02 (0.79–1.33)         | .871       |       | 1.00 (0.76–1.30) | .971 | 0.98 (0.75–1.26) | .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 MELD scores and causes of liver transplantation in addition to all covariates of model 1. CI = confidence interval, HR = hazard ratio, MELD = model for end-stage liver disease.
better prognosis and the adjusted HR of higher education was 0.68 (95% CI: 0.21–2.15).  

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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