Does low income effects 5-year mortality of hepatocellular carcinoma patients?

Dong Jun Kim1,2†, Ji Won Yoo3†, Jong Wha Chang4, Takashi Yamashita5, Eun-Cheol Park6,7, Kyu-Tae Han8, Seung Ju Kim9 and Sun Jung Kim2,10,11*†

Abstract

Background: In Korea, the universal health system offers coverage to all members of society. Despite this, it is unclear whether risk of death from hepatocellular carcinoma (HCC) varies depending on income. We evaluated the impact of low income on HCC mortality.

Methods: The Korean National Health Insurance sampling cohort was used to identify new HCC cases (n = 7325) diagnosed between 2004 and 2008, and the Korean Community Health Survey data were used to investigate community-level effects. The main outcome was 5-year all-cause mortality risk, and Cox proportional hazard models were applied to investigate the individual- and community-level factors associated with the survival probability of HCC patients.

Results: From 2004 to 2008, there were 4658 new HCC cases among males and 2667 new cases among females. The 5-year survival proportion of males was 68%, and the incidence per person-year was 0.768; the female survival proportion was 78%, and the incidence per person-year was 0.819. Lower income was associated with higher hazard ratio (HR), and HCC patients with hepatitis B (HBV), alcoholic liver cirrhosis, and other types of liver cirrhosis had higher HRs than those without these conditions. Subgroup analyses showed that middle-aged men were most vulnerable to the effects of low income on 5-year mortality, and community-level characteristics were associated with survival of HCC patients.

Conclusion: Having a low income significantly affected the overall 5-year mortality of Korean adults who were newly diagnosed with HCC from 2004 to 2008. Middle-aged men were the most vulnerable. We believe our findings will be useful to healthcare policymakers in Korea as well as to healthcare leaders in countries with NHI programs who need to make important decisions about allocation of limited healthcare resources according to a consensually accepted and rational framework.

Keywords: Hepatocellular carcinoma, Liver Cancer, Low income, Mortality, Multi-level analysis, Cox proportional hazard model

* Correspondence: sunjkim0623@sch.ac.kr
† Dong Jun Kim and Ji Won Yoo contributed equally to this work.
2Center for Healthcare Management Science, Soonchunhyang University, Asan, Republic of Korea
3Department of Health Administration and Management, College of Medical Science, Soonchunhyang University, 22 Soonchunhyang-ro, Asan 31538, Republic of Korea
Full list of author information is available at the end of the article

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Background
Mortality rates due to hepatocellular carcinoma (HCC) have tended to increase in many countries in recent decades [1]. In 2018, HCC was the second most common cause of cancer-related mortality in Korea, with a rate of 20.7 per 100,000 [2], which is two- to five-fold higher than in most European countries and the United States [1]. The Korean government has implemented many cancer management policies to identify and resolve these HCC problems [3]. However, the results of the policy were not equal among all HCC patients in Korea [4].

In Korea, HCC is the most common cause of cancer mortality in men aged 40–59 [3]. The consequent economic loss in this age group was estimated to be US$2.8 billion in 2014, which is the largest economic deficit associated with any type of cancer in Korea [3]. Individual-level biological and contextual factors, such as economic conditions, can affect HCC mortality rates [5, 6]. Low income, which is usually defined as the bottom 20% of the income distribution in a country [7], can increase the risk for mortality in HCC patients [5, 6]. Low income is linked to barriers to both formal and informal access to overall healthcare and, in turn, to HCC treatment [8].

Although there have been no nationwide studies on the effects of income on HCC mortality under the universal health system, a study of Ontario [9] residents showed that HCC patients in the lowest income quintile had a 10% higher HCC-related mortality rate than other groups [9].

In terms of socioeconomic factors, access to health insurance is a key factor that enables patients to benefit from the most current treatments [10]. In Korea, under the universal health system, health insurance coverage applies to all members of society. However, individual income is another factor that enables access to health care because, in 2015, the mandatory public health insurance covered only 64% of all healthcare expenditures, leaving 36% of these expenditures to be paid by private supplementary insurance or individuals [7]. Uncovered services included surcharges for specialists at general hospitals, new and high-cost diagnostic or therapeutic services, and private wards [11]. Standard coverage by the National Health Insurance (NHI) can be insufficient for Korean households in general and low-income adults in particular [12]. To increase the financial protection available in the event of catastrophic illness, the Korean government expanded the NHI coverage for cancer patients in 2005; however, the gap between the benefits available to low- and high-income cancer patients remains unchanged [11, 12].

Furthermore, although a few studies have examined the occurrence of and survival following diagnoses of breast, prostate, and colorectal cancer as a function of regional socioeconomic status (SES) [13–16], there has been no comparable HCC-related research. This study investigated the association between low income and HCC mortality at the national level in Korea in the context of community characteristics. We also evaluated whether this association differed by age and sex and estimated the HCC-related mortality risks associated with individual-level demographic characteristics.

Methods
Study population
We used data from the Korean National Health Insurance Service-National Sampling Cohort (NHIS-NSC), which was collected based on a systematic sampling design in 2002–2013, to produce a nationally representative random sample of 1,025,340 individuals, as well as the 2008 Korea Community Health Survey (KCHS) involving data on 200,000 individuals obtained from 253 community health centers [17, 18]. To investigate the associations between individual- and community-level characteristics and survival of HCC patients, we first identified individuals diagnosed with HCC between 2002 and 2013 according to the International Classification of Diseases, version 10 (ICD-10): C22. Then we excluded patients diagnosed during 2002–2003 to ensure that our sample was restricted to newly diagnosed HCC cases under the assumption that, if an individual had no HCC diagnosis in the entire two-year period, then the first diagnosis of HCC from 2004 onward was new. This is because the first diagnosis should be distinguished, taking into account the long disease cycle of cancer. We also excluded patients diagnosed with HCC during 2009–2013 to further restrict the sample to only patients who were followed for 60 months because it is impossible to track the censoring that occurs during this period; this criterion covered patients who were diagnosed during 2004–2008. Then we transposed the dataset into a retrospective cohort design in which the unit of analysis was information from each HCC patient. These claims data consist of a single case of patient medical use. We summarized each case into one patient episode. After that, survival time was measured from the first diagnosis to the time of death, and patients who did not die were defined as survival. To evaluate each HCC patient’s community-level characteristics, we summarized each municipality’s characteristics from individuals of the KCHS, conducted by the Korean Center for Disease Control and Prevention [17, 18]. Furthermore, we matched individual- and community-level data and obtained data on the characteristics of 7325 new HCC patients and their respective 238 municipalities (Fig. 1). This study was reviewed and approved by the Institutional Review Board of Soonchunhyang University (2017–05-BM-014).
Variables
The main outcomes were number of deaths and survival time from HCC over the course of a 5-year follow-up period. The index date was defined as the date of diagnosis. All-cause death data were included in the dataset; however, cause of death could not be identified. Individual-level variables were sex, year of HCC diagnosis, HCC etiology, patient age, income, and disability at diagnosis of HCC. Patient ages were categorized into the following groups (in years): 49 or younger, 50–59, 60–69, and 70 or older. We categorized income into NHI contribution quintiles: 1st quintile (20th or lower percentiles), 2nd quintile (21st–40th percentiles), 3rd quintile (41st–60th percentiles), 4th quintile (61st–80th percentiles), and 5th quintile (80th or higher percentiles) [17, 19]. Data on the status (physical disability or all-cause disability) and severity (grade 1 or 2, severe; grade 3–6, mild) of the disability were provided by the NHIS-NSC based on evaluations performed by the treating physician according to the specific guidelines established by the Korean government [17, 18]. The etiologies of HCC were defined as follows based on ICD-10 coding: HBV, hepatitis c (HCV), alcoholic liver cirrhosis, and other (non-viral non-alcoholic) liver cirrhosis. The KCHS analyzed the following community-level variables in 2008: current smoking rate, high-risk drinking rate, percentage of residents who walk for exercise, obesity rate, and percentage of college graduates. The current smoking rate was defined as the percentage of people who had smoked more than five packs (100 cigarettes) in their lifetime and who were currently smoking (smoked “daily” or “sometimes”). High-risk drinking was defined as consuming seven or more (men) or five or more (women) alcoholic drinks on the same occasion on at least 2 days within the past 7 days. The percentage of residents who walked for exercise was the percentage of people who had walked more than 30 min per day during the last week (7 days). The obesity rate was defined as percentage of people with a body mass index (BMI; kg/m²) greater than 25.

Statistical analyses
We first examined the number and characteristics of individuals newly diagnosed with HCC during the 5-year study period. The frequencies and relative percentages were calculated for categorical variables, and χ² tests were performed to examine differences in each variable by survival. The incidence per person-years and follow-up period were examined as a function of patient characteristics. Also, according to income level, the distribution of deaths and the person-years at deaths were calculated for each variable, and a χ² test was conducted on the distribution. To investigate associations between patient characteristics and death from HCC, after testing
the proportionality assumptions by the Grambsch and Therneau non-proportionality test and log (− log (S (t))) plot, we used Cox proportional hazard models to estimate hazard ratios (HRs) and corresponding 95% confidence intervals (CIs). To identify the individual and community factors associated with the survival probability of HCC patients, we employed a multi-level survival model to include regional-level random effects in an individual model. In addition, subgroup analyses were performed by sex and age groups, trend analysis was performed according to decrease in income level by model, and the threshold for statistical significance was set at $p < 0.05$ (two-tailed) for all analyses. All statistical analyses were performed using SAS statistical software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

**Results**

**Patients and characteristics**

Table 1 presents patient characteristics, number of deaths, and mean survival times. The number of new HCC cases from 2004 to 2008 was stable, with 4658 cases among males and 2667 cases among females. The 5-year survival proportion of males was 68%, and the incidence per person-year was 0.768; the female survival proportion was 78%, and the incidence per person-year was 0.819. The mortality proportion of the highest income group was 25%, while those of the 4th, 3rd, 2nd, and 1st quintiles were 26, 28, 31, and 35%, respectively ($p < 0.001$). Patients with liver cirrhosis had higher mortality rates and shorter survival times than patients without cirrhosis, but an inverse association was found for patients with HBV or HCV. Table 2 shows death information by income level. Table 2 presents, according to income level, the distribution of deaths and the person-years (PY) at deaths. There was a difference in the proportion of deaths and the person-years according to income group (1st quintile: the proportion = 67.2%, PY = 0.670; 2nd quintile: the proportion = 62.2%, PY = 0.669; 3rd quintile: the proportion = 66.9%, PY = 0.852; 4th quintile: the proportion = 62.8%, PY = 0.725; 5th quintile: the proportion = 60.9%, PY = 0.727).

**Risk factors associated with mortality in HCC**

Table 3 shows the hazard ratios of patients with HCC according to both Cox proportional hazard models after adjusting for all other covariates. The HRs of HCC patients increased with age and lower income ($p < 0.001$). However, there were no significant differences between those in the 4th and 5th quintiles of income ($p = 0.161$). Furthermore, HCC patients with HBV, alcoholic liver cirrhosis, and other types of liver cirrhosis had higher HRs than those without these conditions (HBV: HRs = 1.172, $p = 0.001$; alcoholic liver cirrhosis: HRs = 2.187, $p < 0.001$; other liver cirrhosis: HRs = 1.214, $p = 0.023$), but the opposite pattern was found with regard to HCV (HRs = 0.812, $p < 0.001$). The consequences of community factors indicated that higher current smoking rates and a greater percentage of college graduates in the community were associated with higher HRs, and that walking for exercise was associated with lower HRs among HCC patients.

**Subgroup analyses: HCC mortality by sex and age**

Table 4 presents the results of multilevel multivariate analyses of HCC mortality by sex and age. Among male HCC patients, there was a difference in hazard ratio according to income group (1st quintile: HR = 1.422, $p < 0.001$; 2nd quintile: HR = 1.560, $p < 0.001$; 3rd quintile: HR = 1.422, $p < 0.001$; reference group, 5th quintile). Among HCC patients aged 50–59, there was a difference in hazard ratio according to income group (4th quintile: HR = 1.509, $p = 0.010$; 3rd quintile: HR = 1.593, $p = 0.005$; 2nd quintile: HR = 2.089, $p < 0.001$; 1st quintile: HR = 2.197, $p < 0.001$; reference group, 5th quintile), and a significant association also was found in those aged 49 years or younger and 60–69. However, there was no such association among women or those aged 70 years or older who had been diagnosed with HCC.

Table 5 presents the adjusted HRs of HCC mortality for the lowest (1st quintile) and highest (5th quintile, reference) income groups by sex and age considering group interactions. Among male patients, the lowest income group was associated with an increased risk for HCC mortality compared to the highest income group among patients 50–59 years and 49 years or younger (HR = 1.956, $p < .001$ for 49 or younger; HR = 2.678, $p < .001$ 50–59 years). No such association was observed among middle aged female patients ($p = 0.151$ for 49 or younger; $p = 0.734$ 50–59 years).

**Discussion**

Having a low income significantly affected the overall 5-year mortality of Korean adults newly diagnosed with HCC from 2004 to 2008. Middle-aged men with HCC were more vulnerable to the effects of low income on 5-year mortality than were younger and older men and compared to women of all ages.

Our results are similar to those of previous research on the association between health outcomes and SES among HCC patients [20–22]. Although it is difficult to compare health outcomes across health systems, HCC patients living in economically deprived areas in the U.S. are more likely to be diagnosed at an earlier age [20], and those living in the U.K. have a shorter life expectancy [21]. According to nationally representative U.S. cancer registry data, health insurance type (uninsured and Medicaid) and living in low-income communities are associated with worse health outcomes in HCC.
| Variables                        | N/Mean | %/SD | Number of deaths | %    | p*   | Incidence per person-years |
|---------------------------------|--------|------|------------------|------|------|---------------------------|
| Sex                             |        |      |                  |      |      |                           |
| Male                            | 4658   | 63.6 | 1491             | 32%  | <.001| 0.768                     |
| Female                          | 2667   | 36.4 | 576              | 22%  |      | 0.819                     |
| Age group                       |        |      |                  |      |      |                           |
| 49 or younger                   | 2903   | 39.6 | 391              | 13%  | <.001| 0.726                     |
| 50–59                           | 1772   | 24.2 | 395              | 22%  |      | 0.704                     |
| 60–69                           | 1574   | 21.5 | 600              | 38%  |      | 0.769                     |
| 70 or older                     | 1076   | 14.7 | 681              | 63%  |      | 0.888                     |
| Income (quintiles)              |        |      |                  |      |      |                           |
| The 5th (highest)               | 2197   | 30.0 | 549              | 25%  | <.001| 0.810                     |
| The 4th                          | 1649   | 22.5 | 429              | 26%  |      | 0.720                     |
| The 3rd                          | 1310   | 17.9 | 371              | 28%  |      | 0.774                     |
| The 2nd                          | 1083   | 14.8 | 339              | 31%  |      | 0.821                     |
| The 1st (lowest)                | 1086   | 14.8 | 379              | 35%  |      | 0.789                     |
| Disability                      |        |      |                  |      |      |                           |
| None                            | 6751   | 92.2 | 1824             | 27%  | <.001| 0.791                     |
| Mild                            | 459    | 6.3  | 189              | 41%  |      | 0.725                     |
| Severe                          | 115    | 1.6  | 54               | 47%  |      | 0.673                     |
| New cases by year               |        |      |                  |      |      |                           |
| 2004                            | 1478   | 20.2 | 450              | 30%  | 0.033| 0.822                     |
| 2005                            | 1493   | 20.4 | 433              | 29%  |      | 0.776                     |
| 2006                            | 1324   | 18.1 | 387              | 29%  |      | 0.773                     |
| 2007                            | 1352   | 18.5 | 362              | 27%  |      | 0.819                     |
| 2008                            | 1678   | 22.9 | 435              | 26%  |      | 0.727                     |
| Hepatitis B                     |        |      |                  |      |      |                           |
| No                              | 4749   | 64.8 | 1397             | 29%  | 0.002| 0.822                     |
| Yes                             | 2576   | 35.2 | 670              | 26%  |      | 0.708                     |
| Hepatitis C                     |        |      |                  |      |      |                           |
| No                              | 5897   | 82.2 | 1730             | 29%  | 0.036| 0.815                     |
| Yes                             | 1304   | 17.8 | 337              | 26%  |      | 0.643                     |
| Alcoholic liver cirrhosis       |        |      |                  |      |      |                           |
| No                              | 6820   | 93.1 | 1786             | 26%  | <.001| 0.810                     |
| Yes                             | 505    | 6.9  | 281              | 56%  |      | 0.637                     |
| Other (non-viral, non-alcoholic) liver cirrhosis |        |      |                  |      |      |                           |
| No                              | 6895   | 94.1 | 1901             | 28%  | <.001| 0.801                     |
| Yes                             | 430    | 5.9  | 166              | 39%  |      | 0.610                     |
| Regional Level                  |        |      |                  |      |      |                           |
| Current smoking rate †           | 23.6   | 3.0  |                  |      |      |                           |
| High-risk drinking rate †       | 16.4   | 3.7  |                  |      |      |                           |
| Walking exercise practice rate † | 51.8   | 12.2 |                  |      |      |                           |
| Obesity rate †                  | 21.5   | 2.9  |                  |      |      |                           |
| Percentage of college graduates † | 34.2   | 12.6 |                  |      |      |                           |

*p*Chisq-test †Mean/SD
patients [23]. The importance of monitoring and screening populations at risk for HCC, particularly young adults with HBV and/or intravenous drug users, cannot be stressed enough. Economic deprivation and poor access to healthcare likely result in a greater risk for HCC and a shorter survival time. Moreover, among U.S. adults with chronic liver disease (CLD), low income contributed to an increased risk for liver-related mortality [24].

Sudden loss of wealth or a home has been shown to constitute major psychological stressors among U.S. adults [25–27]. Low-income adults with HCC might not be able to afford surcharged services, such as specialty doctors at general hospitals and new and high-cost technology; they also might show lower adherence to prescribed medication regimens and delay needed medical care during the early stages of HCC beyond the NHI coverage deadline [8, 27]. In other words, due to the possible burden of high out-of-pocket expenses, low-income HCC patients might not be able to benefit from new and high-cost diagnostic and therapeutic technology that is not covered by the NHI [11, 12]. The effects of low income on HCC mortality can extend to non-medical domains, particularly among middle-aged adults. Indeed, during the Great Recession of the late 2000s in the U.S., non-medical social welfare spending

| Variables | Income (quintiles) | The 1st (lowest) | The 2nd | The 3rd | The 4th | The 5th (highest) | p* |
|-----------|--------------------|------------------|--------|--------|--------|------------------|----|
|           |                    | %                | %PY    | %      | %PY    | %                |    |
| Sex       |                    |                  |        |        |        |                  |    |
| Male      | 39.4               | 0.763            | 37.0   | 0.853  | 33.4   | 0.776            | 29.8| 0.703| 26.8| 0.772| 0.094|
| Female    | 27.8               | 0.854            | 20.8   | 0.729  | 19.4   | 0.769            | 18.8| 0.779| 22.0| 0.898|        |
| Age group |                    |                  |        |        |        |                  |    |
| 49 or younger | 18.2            | 0.963            | 17.6   | 0.975  | 14.6   | 0.851            | 12.0| 0.731| 9.6  | 0.935| <.001|
| 9         | 29.1               | 0.781            | 28.3   | 0.908  | 22.4   | 0.674            | 22.7| 0.770| 15.5 | 0.774|        |
| 60–69     | 41.8               | 0.701            | 41.1   | 0.760  | 45.2   | 0.801            | 36.1| 0.639| 31.6 | 0.662|        |
| 70 or older | 67.2             | 0.670            | 62.2   | 0.669  | 66.9   | 0.852            | 62.8| 0.725| 60.9 | 0.727|        |
| Disability|                    |                  |        |        |        |                  |    |
| None      | 33.6               | 0.820            | 30.2   | 0.823  | 27.0   | 0.767            | 25.0| 0.736| 23.9 | 0.819| <.001|
| Mild      | 44.8               | 0.747            | 40.8   | 0.742  | 41.4   | 0.761            | 38.1| 0.611| 41.0 | 0.792|        |
| Severe    | 44.8               | 0.453            | 52.6   | 1.039  | 59.1   | 1.088            | 36.4| 0.647| 43.5 | 0.568|        |
| New cases by year |               |                  |        |        |        |                  |    |
| 2004      | 37.2               | 0.816            | 28.1   | 0.765  | 34.9   | 0.697            | 28.9| 0.907| 27.2 | 0.899| 0.002|
| 2005      | 39.2               | 0.687            | 34.0   | 0.947  | 29.7   | 0.828            | 25.7| 0.745| 23.9 | 0.729|        |
| 2006      | 35.6               | 0.925            | 35.5   | 0.883  | 28.1   | 0.732            | 28.7| 0.618| 24.8 | 0.839|        |
| 2007      | 30.7               | 0.911            | 33.0   | 0.734  | 27.6   | 0.944            | 22.1| 0.635| 24.5 | 0.921|        |
| 2008      | 33.0               | 0.729            | 26.3   | 0.774  | 22.8   | 0.725            | 24.4| 0.720| 24.4 | 0.708|        |
| Hepatitis B |                  |                  |        |        |        |                  |    |
| No        | 36.1               | 0.851            | 30.9   | 0.826  | 28.8   | 0.820            | 27.9| 0.729| 26.9 | 0.885| 0.426|
| Yes       | 32.7               | 0.686            | 32.1   | 0.810  | 27.4   | 0.700            | 22.8| 0.702| 21.4 | 0.672|        |
| Hepatitis C |                  |                  |        |        |        |                  |    |
| No        | 35.4               | 0.818            | 31.0   | 0.916  | 28.4   | 0.813            | 27.0| 0.729| 25.7 | 0.837| 0.355|
| Yes       | 32.4               | 0.658            | 32.8   | 0.553  | 27.9   | 0.639            | 21.7| 0.680| 21.6 | 0.686|        |
| Alcoholic liver cirrhosis |             |                  |        |        |        |                  |    |
| No        | 32.3               | 0.854            | 28.3   | 0.860  | 25.6   | 0.782            | 24.0| 0.737| 24.2 | 0.834| <.001|
| Yes       | 62.1               | 0.560            | 63.7   | 0.671  | 56.6   | 0.740            | 51.6| 0.638| 44.0 | 0.579|        |
| Other (non-viral, non-alcoholic) liver cirrhosis | |                  |        |        |        |                  |    |
| No        | 33.6               | 0.809            | 30.6   | 0.831  | 27.7   | 0.803            | 25.6| 0.751| 24.5 | 0.818| 0.420|
| Yes       | 53.6               | 0.643            | 42.9   | 0.715  | 37.5   | 0.551            | 32.1| 0.491| 33.9 | 0.715|        |

*pChisq-test, †Incidence per person-years
provided a social safety net for middle-aged individuals, who generally make larger economic contributions but receive fewer welfare benefits compared to older individuals [28]. The effects of low income on HCC mortality often decrease in later life because of the increased availability of social welfare programs and access to health care with lower amounts of out-of-pocket expenses observed in older individuals [1, 3, 29]. Health behaviors are plausible mediators of health disparities because of social patterning and these influences on health outcomes [30]. Among socially disadvantaged individuals, for example, low-income individuals are prone to be more influenced by sudden loss of wealth or a home, perception of fewer benefits of health behaviors, and pessimistic attitudes of later life [30].

This study had several limitations, and caution is required when interpreting the results and attempting to generalize its findings. Although we analyzed all nationwide inpatient claims for HCC during a defined period, Korea’s unique healthcare delivery and insurance system might significantly limit generalizability of the results to other nations. In addition, given the nature of the health insurance claims dataset, this study retrospectively calculated the time of diagnosis of HCC patients. Although we used the diagnostic information in the claims data, we are confident that the time of diagnosis used in this study reflects the time of actual diagnosis of HCC patients because we reviewed the claims in all available years and excluded the first 2 years of data. However, some degree of measurement error due to unavailability of data on the actual time of diagnosis was unavoidable. Therefore, additional research using cohort data should be performed to verify the associations examined in this study. In addition, potentially important clinical information was not available. For example, we were not able to access the detailed clinical information on HCC patients contained in the health insurance claims data collected by the National Cancer Center. Although we included duration from diagnosis to death or end of follow-up in the analytic models, additional clinical information would have improved the validity of our findings. Additional information, such as cancer stage, site of cancer, and type of cancer, should be considered in future studies to build on our findings and calibrate estimates of the survival probability of HCC patients. In addition, detailed individual- and community-level information on SES was not available for our analyses. For example, it might have been helpful to include educational attainment and income inequality indicators by geographic unit because these can affect the health of both poor and wealthy individuals due to spillover effects (e.g., psychological stress) of income inequality, which can result in erosion of social cohesion [31, 32]. Additional studies should be conducted using a dataset

Table 3 Adjusted hazard ratios of hepatocellular carcinoma mortality by multi-level

| Variables                            | HR (Hazard Ratio) | p-value |
|--------------------------------------|-------------------|---------|
| **Sex**                              |                   |         |
| Female                               | Reference         |         |
| Male                                 | 1.694             | <.001   |
| **Age group**                        |                   |         |
| 49 or younger                        | Reference         |         |
| 50–59                                | 1.691             | <.001   |
| 60–69                                | 3.338             | <.001   |
| 70 or older                          | 8.267             | <.001   |
| **Income (quintiles)**               |                   |         |
| The 5th (highest)                    | Reference         |         |
| The 4th                              | 1.096             | 0.161   |
| The 3rd                              | 1.323             | <.001   |
| The 2nd                              | 1.414             | <.001   |
| The 1st (lowest)                     | 1.451             | <.001   |
| **Disability**                       |                   |         |
| None                                 | Reference         |         |
| Mild                                 | 1.144             | 0.084   |
| Severe                               | 1.454             | 0.008   |
| **New cases by year**                |                   |         |
| 2004                                 | Reference         |         |
| 2005                                 | 0.949             | 0.441   |
| 2006                                 | 1.030             | 0.675   |
| 2007                                 | 0.933             | 0.336   |
| 2008                                 | 0.914             | 0.192   |
| **Hepatitis B**                      |                   |         |
| No                                   | Reference         |         |
| Yes                                  | 1.172             | 0.001   |
| **Hepatitis C**                      |                   |         |
| No                                   | Reference         |         |
| Yes                                  | 0.812             | <.001   |
| **Alcoholic liver cirrhosis**        |                   |         |
| No                                   | Reference         |         |
| Yes                                  | 2.187             | <.001   |
| **Other (non-viral, non-alcoholic) liver cirrhosis** | | |
| No                                   | Reference         |         |
| Yes                                  | 1.214             | 0.023   |
| **Regional Level**                   |                   |         |
| Current smoking rate *               | 1.019             | 0.038   |
| High-risk drinking rate *            | 0.994             | 0.331   |
| Walking exercise practice rate *     | 0.996             | 0.037   |
| Obesity rate *                       | 1.003             | 0.634   |
| Percentage of college graduates *    | 1.005             | 0.023   |
| Income †                            | 1.106             | <.001   |

*Continuous variable at regional level † Trend test according to decrease in income level
## Table 4 Adjusted hazard ratios of hepatocellular carcinoma mortality by sex and age groups

| Variables          | Income (quintiles) | Hazard ratio | 95% Hazard ratio confidence limits | p-value |
|--------------------|--------------------|--------------|-----------------------------------|---------|
| **Male**           |                    |              |                                   |         |
|                    | The 5th (highest)  | Reference    |                                   |         |
|                    | The 4th            | 1.140        | 0.979 to 1.328                    | 0.092   |
|                    | The 3rd            | 1.422        | 1.212 to 1.669                    | <.001   |
|                    | The 2nd            | 1.560        | 1.325 to 1.838                    | <.001   |
|                    | The 1st (lowest)   | 1.541        | 1.309 to 1.815                    | <.001   |
|                    | Trend test†        | 1.127        | 1.087 to 1.169                    | <.001   |
|                    | Female             |              |                                   |         |
|                    | The 5th (highest)  | Reference    |                                   |         |
|                    | The 4th            | 1.033        | 0.810 to 1.318                    | 0.794   |
|                    | The 3rd            | 1.107        | 0.857 to 1.429                    | 0.436   |
|                    | The 2nd            | 1.129        | 0.862 to 1.477                    | 0.379   |
|                    | The 1st (lowest)   | 1.265        | 0.995 to 1.607                    | 0.055   |
|                    | Trend test†        | 1.057        | 1.000 to 1.118                    | 0.049   |
|                    | Age 49 or younger  |              |                                   |         |
|                    | The 5th (highest)  | Reference    |                                   |         |
|                    | The 4th            | 1.270        | 0.929 to 1.735                    | 0.135   |
|                    | The 3rd            | 1.595        | 1.166 to 2.181                    | 0.004   |
|                    | The 2nd            | 1.714        | 1.239 to 2.371                    | 0.001   |
|                    | The 1st (lowest)   | 1.568        | 1.121 to 2.193                    | 0.009   |
|                    | Trend test†        | 1.131        | 1.052 to 1.215                    | 0.001   |
|                    | Age 50–59          |              |                                   |         |
|                    | The 5th (highest)  | Reference    |                                   |         |
|                    | The 4th            | 1.509        | 1.105 to 2.059                    | 0.010   |
|                    | The 3rd            | 1.593        | 1.151 to 2.204                    | 0.005   |
|                    | The 2nd            | 2.089        | 1.512 to 2.887                    | <.001   |
|                    | The 1st (lowest)   | 2.197        | 1.586 to 3.043                    | <.001   |
|                    | Trend test†        | 1.209        | 1.126 to 1.298                    | <.001   |
|                    | Age 60–69          |              |                                   |         |
|                    | The 5th (highest)  | Reference    |                                   |         |
|                    | The 4th            | 1.116        | 0.875 to 1.423                    | 0.377   |
|                    | The 3rd            | 1.474        | 1.147 to 1.895                    | 0.003   |
|                    | The 2nd            | 1.355        | 1.036 to 1.772                    | 0.026   |
|                    | The 1st (lowest)   | 1.354        | 1.044 to 1.757                    | 0.022   |
|                    | Trend test†        | 1.087        | 1.026 to 1.150                    | 0.004   |
|                    | Age 70 or older    |              |                                   |         |
|                    | The 5th (highest)  | Reference    |                                   |         |
|                    | The 4th            | 0.967        | 0.777 to 1.202                    | 0.759   |
|                    | The 3rd            | 1.140        | 0.894 to 1.454                    | 0.292   |
|                    | The 2nd            | 1.074        | 0.841 to 1.372                    | 0.569   |
|                    | The 1st (lowest)   | 1.177        | 0.945 to 1.466                    | 0.146   |
|                    | Trend test†        | 1.042        | 0.991 to 1.096                    | 0.111   |

*All adjusted by sex, age group, disability, new cases by year, hepatitis B, hepatitis C, alcoholic liver cirrhosis, other (non-viral, non-alcoholic) liver cirrhosis and regional level (current smoking rate, high-risk drinking rate, walking exercise practice rate, obesity rate, percentage of college graduates). †Trend test according to decrease in income level.*
with more detailed matching of NHI claims data as well as more information on SES.

Despite these limitations, to the best of our knowledge, this is the one of only a few studies to analyze the Korean national claims dataset of HCC patients and to explore individual- and community-level factors associated with the survival probability of these individuals.

Conclusions
Having a low income significantly affected the overall 5-year mortality of Korean adults who were newly diagnosed with HCC from 2004 to 2008. Middle-aged men were the most vulnerable. We believe our findings will be useful to healthcare policymakers in Korea as well as to healthcare leaders in countries with NHI programs who need to make important decisions about allocation of limited healthcare resources according to a consensually accepted and rational framework. Our findings also add to the mounting empirical support for development of a national cancer management strategy to narrow the gaps in, for example, survival time and access to healthcare according to demographic characteristics, including SES.

Abbreviations
HCC: Hepatocellular Carcinoma; HR: Hazard Ratio; HBV: Hepatitis B; HCV: Hepatitis C; NHI: National Health Insurance; SES: Socioeconomic Status; NHIS-NSC: Korean National Health Insurance Service-National Sampling Cohort; KCHS: Korea Community Health Survey; ICD-10: International Classification of Diseases, Version 10; BMI: Body Mass Index; PY: Person-Years; CI: Confidence Interval; CLD: Chronic Liver Disease; NRF: National Research Foundation of Korea

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Sun Jung Kim is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Authors’ contributions
DJK, JWY, and Sun Jung Kim led the design and conception of the study, performed the data analysis, and wrote the manuscript. JWC, TY, ECP, KTH, and Seung Ju Kim contributed to the discussion, reviewed and edited the manuscript. The authors read and approved the final manuscript.
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Availability of data and materials
The data generated by the National Health Insurance Corporation, Republic of Korea, are not publicly available.

Declarations

Ethics approval and consent to participate
This study was reviewed and approved by the Institutional Review Board of Soonchunhyang University (2017–05-MA-014). The English in this document has been checked professional editors.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
1Department of Health Administration and Management, Soonchunhyang University Graduate School, Asan, Republic of Korea. 2Center for Healthcare Management Science, Soonchunhyang University, Asan, Republic of Korea. 3Department of Internal Medicine, University of Nevada Las Vegas School of Medicine, Las Vegas, Nevada, USA. 4Department of Health Administration and Management, College of Business, Texas Women’s University, Denton, TX, USA. 5Department of Sociology, Anthropology, and Health Administration and Policy, University of Maryland, Baltimore, MD, USA. 6Department of Preventive Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea. 7Institute of Health Services Research, Yonsei University College of Medicine, Seoul, Republic of Korea. 8Department of Community Health and Nursing, Catholic University of Korea, Seoul, Republic of Korea. 9Division of Cancer Management Policy, National Cancer Center, Goyang, Republic of Korea. 10College of Nursing, Catholic University of Korea, Seoul, Republic of Korea. 11Department of Health Administration and Management, College of Medical Science, Soonchunhyang University, Seoul 22 Soonchunhyang-ro, Asan 31538, Republic of Korea. 12Department of Software Convergence, Soonchunhyang University, Asan, Republic of Korea.

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