Original article

High combined individual and neighborhood socioeconomic status correlated with better survival of patients with lymphoma in post-rituximab era despite universal health coverage

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A R T I C L E   I N F O

A B S T R A C T

The correlation between high socioeconomic status (SES) and better survival outcome in patients with either Hodgkin lymphoma (HL) or non-Hodgkin lymphoma (NHL) was well-established in the pre-rituximab era. However, whether or not such an association exists in the post-retuxamib era has not been reliably demonstrated. Herein we conducted a population-based study in Taiwan involving 5010 patients diagnosed between 2002 and 2006 to investigate the relationship between individual and neighborhood SES and survival outcomes for lymphoma. A proxy measure of individual SES is based on income-related insurance payment, and neighborhood SES is based on neighborhood household income.

After adjusting for patient characteristics, treatment modalities, and hospital characteristics, HL patients with high individual SES in advantaged neighborhoods showed a decreased risk of mortality (HR 0.33, 95%, CI 0.10–0.99). NHL patients with high individual SES in advantaged neighborhoods showed a moderate decreased risk of death (HR 0.62; 95% CI 0.51–0.75), compared to those with low SES in disadvantaged neighborhoods. In the future, public health strategies and welfare policies must continue to focus on this vulnerable group.

1. Introduction

In Taiwan, hematologic malignancies have become increasingly prevalent during recent decades,[1,2] especially non-Hodgkin lymphoma. According to a report from the Taiwan Cancer registry, more than 80% of non-Hodgkin lymphoma patients suffered from the B-cell type disease.[3] Since its approval by the Taiwan FDA in 2002, rituximab had been the most commonly prescribed drug used in combination with multi-agent chemotherapy for most patients with CD20-positive B-cell lymphoma. In the United States, based upon "real world" investigation, patient survival outcome significantly improved in the post-rituximab era[4]; yet this new era has caused moving target-like results when trying to predict the prognosis of patients with lymphoma. While earlier models relied mainly on disease character, host character, and biomarker models, there was a distinct lack of socioeconomic models used to assess patient survival.[5]

In the pre-rituximab era, a growing body of literature suggests a persistent positive relationship existed between socioeconomic status (SES) and health status, with high SES correlating with better survival outcome in lymphoma, including Hodgkin and non-

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Hodgkin types.[6–9] But the impact of SES on lymphoma survival in the post-rituximab era remains unconfirmed. SES is thought to impact cancer survival via various mechanisms, which was briefly divided into those aspects of disease or host, including but not limited to delayed diagnosis, differential health-seeking behavior, access to care, and the presence of co-morbid conditions, among other factors.[10–14] According to a previous study focusing on patient SES, insurance coverage played an important role in health inequity. However, universal health coverage in Taiwan might have eliminated the practice of altering treatment modalities among patients with different SES.

Otherwise, to limit the proxies of SES, several studies have explored the combined or cross-level interaction effect of individual SES and neighborhood SES in several malignancies[15–17]; however, several of these studies have shown conflicting results.[18,19] To date, there has been no large-scale study which explored the combined effect of individual and neighborhood SES on lymphoma.

This article describes and compares the overall survival rates and relative risk of death in patients who were diagnosed with lymphoma in the post-rituximab era, from 2002 to 2006. We used the Taiwan National Health Insurance Research Database (NHIRD), census data, and public information from the Department of Health to extract individual patient SES and neighborhood SES data. We used a population-based data set merged with neighborhood SES information to measure the contextual effect of individual and neighborhood SES on lymphoma survival rates.

2. Materials and methods

2.1. Ethics statement

This study was initiated after being approved by the Research Ethical Committee of Buddhist Dalin Tzu Chi General Hospital. All identifying personal information was removed from the secondary files prior to analysis, and the review board agreed to waive the requirement for written informed consent from the patients involved.

2.2. Database

The data for this study originated from the NHIRD in Taiwan between 2002 and 2006. The National Health Insurance Program enrolls up to 99% of the Taiwanese population and contracts with 97% of Taiwanese medical providers.[20,21] The study cohort consisted of patients with lymphoma who began treatment between 2002 and 2006. Lymphoma cases were assigned to one of two primary diagnostic groups: Hodgkin lymphoma and non-Hodgkin lymphoma, based on coding numbers from ICD-9 (Hodgkin lymphoma: 201, Non - Hodgkin lymphoma: 200 & 202).

2.3. Measurements

We observed that the key dependent variable of interest was the 5-year survival rate. The overall survival rate was utilized because it was not possible to determine cause-specific survival rates based on this registry data.[22] The key independent variables were the contextual effects of individual SES and neighborhood SES. Patients were then linked to the mortality data covering the years 2002–2011 to calculate overall survival duration. Each patient was tracked from his or her first curative treatment for a five-year period using administrative data to identify all patients who died during the study period. Patient characteristics included age, gender, geographic location, treatment modality, severity of co-morbidity, and monthly income. The severity of co-morbidity of each patient was based on the modified Charlson Comorbidity

Index Score (CCIS), which has been widely accepted for risk adjustment in administrative claims data sets.[23]

2.4. Individual-level measures

This study used the income-related insurance payment amount as a proxy measure of individual SES at the time of diagnosis, which is an important prognostic factor for cancer.[24] By recursive partitioning analysis, we found that NT$ 25000 was an ideal cut-off point for stratifying our cohort in terms of SES. The cancer patients were classified into two groups: 1) low SES: lower than US $821 (New Taiwan Dollar (NT$) 25000) per month; and 2) high SES: US $821 (NT$25001) or more per month, as in our previous studies.[15–17,25]

2.5. Neighborhood-level socioeconomic status

For neighborhood SES, household income is a contextual characteristic representing averages and percentages measured at the enumeration level in the 2001 Taiwan Census. Neighborhood household income was measured using per capita personal income by township acquired from the 2001 income tax statistics released by Taiwan's Ministry of Finance (http://www.fdc.gov.tw/dp.asp?mp=5).[15] Advantaged and disadvantaged neighborhoods were identified based on the median values of neighborhood characteristics, with advantaged neighborhoods having higher-than-median neighborhood household incomes, US$ 17900 (or NT $537000), and disadvantaged neighborhoods having lower-than-median household incomes.

2.6. Other variables

The urbanization levels of residences were classified into 7 levels based upon 5 indices: population density, percentage of residents with college level or higher education, percentage of residents >65 years of age, percentage of residents who were agricultural workers, and the number of physicians per 100,000 people.[26] We recorded the urbanization level of residences as urban (urbanization level 1), sub-urban (urbanization levels 2–3), or rural (urbanization levels 4–7).

The hospitals were categorized by ownership (public, nonprofit, or for-profit), and hospital level (medical center, regional or district hospital). The geographic regions where the cancer patients resided were recorded as Northern, Central, Southern and Eastern Taiwan.

2.7. Statistical analysis

The SPSS program (version 15, SPSS Inc., Chicago, IL, USA) was used for data analysis. Pearson's chi-square test was used for categorical variables such as gender, level of urbanization, geographic region of residence, CCIS, treatment modality, and hospital characteristics, and continuous variables were analyzed with one-way ANOVA.

The cumulative 5-year survival rates and the survival curves were constructed and compared using the log-rank test. Survival curves, stratified by individual SES and neighborhood SES, were measured from the time of diagnosis by using overall mortality as the event variable. The Cox proportional hazards regression model adjusted for patients' characteristics (age, gender, CCIS, urbanization and area of residence), treatment modality and hospital characteristics, was used to compare outcomes between different SES categories. SES variables were introduced into the Cox model, with the high individual SES and advantaged neighborhood group as the reference group. A two-tailed P-value ($P < 0.05$) was used to determine statistical significance.