

BMJ Open Influence of social determinants of health on patients with advanced lung cancer: a prospective cohort study

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ABSTRACT

Introduction Socioeconomic factors with an influence on human health are known as social determinants of health (SDH). There are some SDH studies in patients with lung cancer, but important exposures such as social isolation and loneliness have not been adequately investigated. This study will assess the influence of SDH, particularly social isolation and loneliness, on patients with advanced lung cancer in Japan.

Methods and analysis The inclusion criteria for this prospective cohort study will be as follows: a diagnosis of advanced lung cancer; unsuitability for curative surgery; and willingness to participate. The primary outcome will be the initial choice of treatment and the secondary outcomes will be overall survival, changes in disease staging or performance status, route to diagnosis and place of death. The exposures will be social isolation, loneliness, employment, insurance type, education and dementia. The study enrolment period will be 1 year and the follow-up duration will be 2 years. The log-rank test will be used to compare overall survival between patients when grouped according to the study exposures and multivariate analysis will be performed using Cox proportional hazards regression. The X^2 test will be used to compare the initial treatment, changes in disease stage and place of death, and logistic regression will be used for multivariate analysis of these factors. A p value <0.05 will be considered statistically significant.

Ethics and dissemination This study has been approved by the Institutional Review Board at Hyogo Prefectural Amagasaki General Medical Center (No 29-164). A manuscript summarising the outcome of this study will be submitted to a peer-reviewed journal and the data will be presented at conferences.

Trial registration number UMIN000031810.

INTRODUCTION

Socioeconomic factors have an effect on human health and are known as social determinants of health (SDH).¹ The College of Family Physicians of Canada defines SDH to include income, education, unemployment, job security, working conditions,

Strengths and limitations of this study

- This will be the first study to evaluate the influence of social determinants of health on patients with lung cancer in Japan.
- The study will determine the relationship between social factors and treatment, which may be useful in terms of refining social welfare policy.
- A limitation of this study will be that patients who only visit the hospital once will not be followed up.

early childhood development, race, gender, sexuality, food insecurity, housing, social exclusion, social safety, net, health services, indigenous status and disability.¹ Many studies dating back as far as the early 20th century have addressed these issues.¹ The WHO recognises the importance of SDH for health equality, and an international conference on SDH was held in Rio De Janeiro in 2011.²

Social isolation and loneliness are key issues in SDH. According to Holt-Lunstad *et al*,³ social isolation is ‘an objective and quantifiable reflection of reduced social network size and paucity of social contact’ and consists of family and friendship components.⁴ Loneliness is ‘the psychological embodiment of social isolation, reflecting the individual’s experienced dissatisfaction with the frequency and closeness of their social contacts or the discrepancy between the relationships they have and the relationships they would like to have.’³ A systematic review showed that social isolation and loneliness lead to high mortality regardless of the presence or absence of medical conditions.³ These two factors have been reported to lead to poor health behaviours, including cigarette smoking, excessive alcohol consumption and poor sleep, which in turn lead to health problems such as high blood pressure

and poor immune function.⁵ Being disconnected from society has a negative effect on the individual psychologically and physically.

There has been some relevant research in patients with lung cancer. For example, a cohort study in patients with lung cancer showed that being uninsured was associated with shorter survival; however, the study sample was limited to patients with small cell lung cancer.⁶ There have also been some systematic reviews of SDH in patients with lung cancer, but factors such as social isolation and loneliness were not addressed.⁷ To the best of our knowledge, no study has investigated the impact of social isolation and loneliness in patients with lung cancer.

We will conduct this study to assess the effects of SDH on patients with advanced lung cancer in Japan.

METHODS AND ANALYSIS

Study design

This will be a prospective cohort study conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement.⁸

Setting

A tertiary hospital (Hyogo Prefectural Amagasaki Medical Center).

Participants

Inclusion criteria:

1. A pathological or clinical diagnosis of lung cancer.
2. Willingness to provide written informed consent for enrolment in the study.
3. Unsuitability for curative surgery.
4. Previously untreated or within 2 months of starting treatment for newly diagnosed lung cancer.

Exclusion criteria:

1. Inability to complete a study questionnaire because of dementia or mental illness.
2. Unsuitable for participation in the study in the opinion of the attending physician.

Study variables

The primary outcome will be the initial treatment provided. The secondary outcomes will be overall survival, stage of cancer progression and performance status at the time of enrolment, route to diagnosis and place of death. All outcomes will be surveyed at the end of the follow-up period except for performance status.

Overall survival will be defined as the interval between diagnosis and death. Staging will be undertaken either before or after enrolment in the study but will only be required if clinically meaningful.

Chemotherapy, radiotherapy and radical surgery within 3 months of enrolment will be defined as active therapy. If none of these treatments are undertaken, the patient will be defined as receiving best supportive care, which will also include palliative radiotherapy and any uninsured treatment. Route to diagnosis refers to how the patient

first came to visit a hospital and includes health examination, an outpatient attendance and emergency presentation. Place of death, that is, whether the patient dies at home, in a nursing home, hospital or a palliative care unit, will be recorded. For the analysis, the place of death will be classified as 'at home' or 'in a facility'.

The exposures in this study will be social isolation, loneliness, employment, social security income, education, depression, anxiety and dementia. The confounding factors for the prognosis will be smoking history, weight loss, respiratory symptoms, tissue type, cancer staging (eighth edition of the tumour-node-metastasis classification devised by the American Joint Commission on Cancer and the Union for International Cancer Control),⁹ mutation status (epidermal growth factor receptor, anaplastic lymphoma kinase, ROS1) and programmed death ligand 1 status.

Social isolation will be surveyed using the Japanese short version of the Lubben Social Network Scale (LSNS-6).¹⁰ It does not have a cut-off level, so we use English cut-off level and it is 12 out of 30 points.¹⁰ Loneliness will be surveyed using the Japanese version 3 of the University of California, Los Angeles (UCLA) Loneliness Scale.^{11 12} Dementia will be surveyed using questions quoted from the Life Function Evaluation for Care Provision.¹³ These instruments will be administered at the time of enrolment. Depression and anxiety are surveyed from medical records.

Sample size

Rowland and Lyons reported that people who live alone are likely to be financially poorer than their married counterparts.¹⁴ Furthermore, a systematic review found that patients of lower socioeconomic status had a reduced likelihood of receiving any form of treatment (OR 0.79).⁶ For example, if 70% of patients in a socially isolated group and 54% of patients in a non-isolated group were receiving active therapy, the significance level was 5%, and the probability of type II error was 20%, the required sample size would be 306 patients. Our hospital treats approximately 300 new patients with advanced or recurrent lung cancer annually. Allowing for non-eligible patients, the enrolment period will be 18 months. The follow-up period will be 2 years.

Procedure

Contributing researchers and a clinical research coordinator (CRC) will identify eligible patients and inform the attending doctors. The doctors will provide the consent forms and questionnaires. After the forms are completed, a doctor or nurse will collect the documents. The CRC will keep the documents and the data entered into a computer in a locked room. During the follow-up period, the CRC will check all items from the charts at 3-month intervals. If a patient is referred to another institution, a researcher will ask that institution about the patient's prognosis.

Statistical methods

The statistical analysis will be performed using EZR V.1.33 software (Saitama Medical Center, Jichi Medical University, Japan).¹⁵ The log-rank test will be used to compare overall survival between the patient groups, and Cox proportional hazards regression will be used for the multivariate analysis. The X^2 test will be used to compare the initial treatment provided, any change in disease staging and place of death, and logistic regression analysis will be used for the multivariate analysis. A p value <0.05 will be considered statistically significant. The multiple imputation method will be used to account for missing data.

Patient and public involvement statement

We did not have any research question and outcome measures by patients. Any patients did not involve in the design and recruitment of this study. Therefore, there are not any patient advisers to be thanked in the contributorship statement. We will put the result of this study on our institution's homepage.

ETHICS AND DISSEMINATION

This human study has been approved by the Institutional Review Board (IRB) of Hyogo Prefectural Amagasaki General Medical Center (No 29-164) and will be conducted in accordance with the tenets of the Declaration of Helsinki. If the protocol requires revision at a later date, IRB approval will be required.

The attending physician will explain the nature of the research to each patient and obtain written informed consent for inclusion in the study. The CRC will keep the consent forms and enrolment documents in a locked cupboard in the hospital.

There will be no health risk as a consequence of participation in this study, so no compensation plan is required.

The principal investigator will have access to the final data set. A manuscript summarising the results of the study will be submitted to a peer-reviewed journal and the data will be presented at conferences. The principal investigator meets the criteria for authorship and there is no plan to engage a professional writer to report on the study.

DISCUSSION

The influence of SDH on patients with lung cancer is obvious. However, as far as we are aware, this will be the first study to evaluate the influence of social isolation and loneliness on patients with lung cancer. Previous reports^{6 7} suggest that these factors are associated with higher mortality. If the results of this study show a negative relationship between social factors and choice of treatment, this would be useful information in terms of developing social support strategies as part of care for patients with advanced lung cancer.

This study will have some limitations. First, there will be a degree of selection bias in that some patients will

not be accessible for potential recruitment. To minimise this shortcoming, the CRC will identify patients with a new pathological diagnosis of lung cancer because the attending doctors are unlikely to have enough time available for recruitment of patients. Eligible patients with newly diagnosed lung cancer who are hospitalised will be identified by the doctors at the weekly hospital conference. However, some degree of selection bias will be unavoidable. For example, some patients with high income are likely to attend specialist hospitals in other regions and receive highly advanced medical treatment. This bias may weaken the relationship between social factors and treatment or prognosis. However, the proportion of patients with high income should be negligible. Furthermore, the patients of our hospital are thought to be the representative population of our region, considering the situation that most of the patients go to the hospital where they live, and our facility is a tertiary hospital with 730 beds. Second, we will use a short patient-friendly questionnaire to evaluate loneliness and dementia. The Japanese version 3 of the UCLA Loneliness Scale is already validated.^{12 16} However, the Japanese version of the abbreviated LSNS-6 does not have a fixed cut-off level, so we will use the cut-off level for the English version, and we will use the median value for the sensitivity analysis.¹⁰ The Life Function Evaluation for Care Provision has been verified with the Clinical Dementia Rating used to assess dementia in six domains (eg, memory and orientation). The criterion-related validity of the Clinical Dementia Rating is confirmed using the Mini-Mental State Examination.¹⁷

In conclusion, this is the first study to investigate SDH in terms of social isolation and loneliness in patients with lung cancer in Japan. We anticipate that its findings will have an impact on the social aspects of care provided for these patients in Japan.

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Contributors TT, YK and NT were responsible for the conception, design and protocol writing. TT and YK analysed the data and wrote the manuscript. All the authors except for TN (KO, AS, TI, SI, ES, HT, HM, SK, NW, MS, TO, TT, MS, JN, RI, YK, KH, TH, KE, MH) supported the conception and acquisition of data, and collected the data. All the authors approved the final version of this protocol before submission.

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Competing interests KH has received lecture fees from AstraZeneca; Chugai Pharmaceutical, Eli Lilly; Nippon Boehringer Ingelheim, Ono Pharmaceutical, Pfizer; Taiho Pharmaceutical and Novartis. JN has received lecture fees from Eli Lilly. MS has received lecture fees from MSD and Eli Lilly. TM has received lecture fees from Ono Pharmaceutical and AstraZeneca.

Patient consent Obtained.

Ethics approval Institutional Review Board of Hyogo Prefectural Amagasaki General Medical Center (No 29-164).

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