Cancer Epidemiology 47 (2017) 100–105

Contents lists available at ScienceDirect

Cancer Epidemiology

The International Journal of Cancer Epidemiology, Detection, and Prevention

journal homepage: www.cancerepidemiology.net

Original Research Article

Lymphohaematopoietic malignancies in Scottish military veterans: Retrospective cohort study of 57,000 veterans and 173,000 non-veterans

Beverly P. Bergman*, Daniel F. Mackay, Jill P. Pell

Institute of Health and Wellbeing, University of Glasgow, Glasgow G12 8RZ, UK

ARTICLE INFO

Article history:
Received 26 July 2016
Received in revised form 14 December 2016
Accepted 6 February 2017
Available online 23 February 2017

Keywords:
Veterans
Military
Leukaemia
Hodgkin lymphoma
Non-Hodgkin lymphoma
Retrospective cohort study

ABSTRACT

Background: Lymphohaematopoietic malignancies are common in the general population. There have been concerns that military service may be associated with increased risk as a result of occupational exposures. To date, few studies have demonstrated an increased risk, although a disability pension is payable to veterans who were present at nuclear tests and who develop leukaemia (other than chronic lymphocytic leukaemia). The aim of the study was to utilise data from the Scottish Veterans Health Study to examine the risk of lymphohaematopoietic malignancy following military service in a large national cohort of veterans.

Methods: Retrospective cohort study of 57,000 veterans and 173,000 non-veterans born between 1945 and 1985 matched for age, sex and area of residence, adjusted for areal deprivation and followed up for up to 30 years, using Cox proportional hazard models to compare the risk of lymphohaematopoietic malignancy overall, by diagnosis and by sex and birth cohort.

Results: We found no statistically significant difference in risk between veterans and non-veterans either for all leukaemias (Cox proportional hazard ratio 1.03, 95% confidence intervals 0.84–1.27, p = 0.773), Hodgkin lymphoma (hazard ratio 1.19, 95% confidence intervals 0.87–1.61, p = 0.272) or for non-Hodgkin lymphoma (hazard ratio 0.86, 95% confidence intervals 0.71–1.04, p = 0.110).

Conclusion: Our findings provide reassurance that service in the UK Armed Forces is not associated with increased risk of lymphohaematopoietic malignancy.

1. Background

1.1. Introduction

Lymphohaematopoietic malignancies are common in the general population, leukaemia accounting for 3% of all new cancers, with an age-standardised incidence rate of 10.2 per 100,000 per year in the UK. In addition there are 15.1 cases of non-Hodgkin lymphoma per 100,000 population (4% of all new cancers), whilst Hodgkin lymphoma accounts for a further 2.9 cases per 100,000 per year. The lymphomas are the second most common cancers in male adolescents and young adults, whilst leukaemia is the fourth commonest [1]. Concerns have been expressed that occupational exposures, especially to ionising radiation [2], fuels [3], and electromagnetic fields [4] may result in increased risk in military personnel. In 1980, a US report linked nine cases of leukaemia to participation in military exercises during the 1957 nuclear test explosion [5]. In 2001, it was reported that military service in the Balkans may have been associated with an increased risk of leukaemia as a consequence of the use of depleted uranium munitions some five years earlier, following the deaths of six Italian soldiers who had served there [6]. By contrast, studies of Porton Down veterans who took part in tests of chemical warfare agents between 1941 and 1989 showed no statistically significant difference in risk of leukaemia or other lymphatic or haematopoietic cancer in comparison with unexposed veterans [7]. Overall, formal epidemiological evidence has provided a conflicting picture, with most studies reporting no increased risk associated with either radiation [8], or exposure to electromagnetic fields (4) in military personnel.

* *Corresponding author at: Institute of Health and Wellbeing, Public Health & Health Policy, 1 Lilybank Gardens, Glasgow, G12 8RZ, UK.
E-mail addresses: Beverly.bergman@glasgow.ac.uk (B.P. Bergman), Jill.pell@glasgow.ac.uk (J.P. Pell).

http://dx.doi.org/10.1016/j.canep.2017.02.001
1877-7821/

1.2. Military risks

Assessing occupational exposures in military personnel presents challenges as there are few official records. Exposure records are especially likely to be suboptimal during conflict, when risks may be greatest [9]. Both training and deployed operational service may involve exposure to a wide range of potentially hazardous substances; although these are controlled wherever practicable, some exposures inevitably remain [10]. Therefore, examination of the impact of military service overall on the risk of lymphohaematopoietic cancer is particularly important, but there have been few long-term studies on UK personnel. The Scottish Veterans Health Study provided an opportunity to examine the risk of leukaemia, Hodgkin lymphoma and non-Hodgkin lymphoma in a large national cohort of military veterans irrespective of military experience and exposures, in comparison with age, sex and geographically matched people with no record of military service, in order to examine whether military service overall was associated with increased risk.

2. Methods

2.1. General

The Scottish Veterans Health Study is a retrospective cohort study of all 56,570 military veterans (male and female) who were resident in Scotland and registered for NHS care before and after military service, and who were born between 1 January 1945 and 31 December 1985, and a comparison group of 172,753 individuals with no record of service matched 3:1 for age, sex and postcode sector of residence (mean population 5000). The cohort was identified from the NHS Scotland database, which covers the entire Scottish population and includes dates of military service where relevant. Individuals were included as 'veterans' if they had both 'Exit to Armed Forces' and 'From Armed Forces' ciphers on the NHS record; they were categorised as 'non-veterans' if both ciphers were absent. Those having only one of the two ciphers were excluded from both groups as their veteran status could not be established with certainty. The study cohort and methods have been fully described elsewhere [11]. Demographic data obtained from electronic NHS registration records were electronically linked at an individual level to routine hospital admissions data (Scottish Morbidity Record SMR01), cancer registrations (SMR06), and death certificates to provide information on first episode of leukaemia, Hodgkin lymphoma and non-Hodgkin lymphoma (hospitalisation or death) and all-cause death. The NHS demographic record provided dates of entering and leaving the Service for veterans. The maximum period of follow-up was from 1 January 1981 (or date of leaving the Service, for veterans, if later) to 31 December 2012. The data extract was pseudo-anonymised and approval for the study was granted by the Privacy Advisory Committee of the Information Services Division of NHS Scotland.

2.2. Deprivation

Details of the Scottish Index of Multiple Deprivation (SIMD) are published by the Scottish Government [12]. In Scotland, there are 6505 datazones, based on postcode of residence, with a mean population of 800. The Scottish Index of Multiple Deprivation (SIMD) for each datazone is derived from information on income, employment, health, education (including skills and training), housing, crime, and access to services. The SIMD has been used to derive quintiles of areal deprivation for the Scottish population; ranging from 1 (most deprived) to 5 (least deprived). We used postcode of residence to categorize the cohort participants according to these quintiles.

2.3. Statistical analyses

'Leukaemia' was defined as ICD-10 C90-C95 and ICD-9 203–208, 'Hodgkin lymphoma' as ICD-10 C81 and ICD-9 201 and 'non-Hodgkin lymphoma' as ICD-10 C82-C85 and ICD-9 200 and 202, at any position in the record. Cox proportional hazard models were used to examine the association between veteran status and cumulative risk of any of these lymphohaematopoietic cancers, combined and separately, using age as the time dependent variable, age at first recorded occurrence as the failure time and death (if no lymphohaematopoietic cancer) as the censor time. The *a priori* rejection level was set at 0.05. Cox proportionality assumptions were tested using methodology based on Schoenfeld residuals [13]. The log-likelihood test was used to test for interactions with sex and birth cohort. A landmark analysis was performed using age 20 years as the starting point in order to exclude people with a history of childhood leukaemia or lymphoma, which would have precluded military service. The models were run univariately and then repeated adjusting for the potential confounding effect of deprivation. The analyses were repeated stratifying by grouped year of birth to examine potential birth cohort effects. Cox proportional hazard models were used to compare case-fatality one and five years following diagnosis between veterans and non-veterans. All analyses were performed using Stata v12.1 (©1985–2011 StataCorp).

2.4. Role of the funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

3. Results

3.1. Descriptive epidemiology

After data cleansing, 56,205 (99.3%) veterans and 172,741 (99.9%) non-veterans were included in the analysis. There were 50,970 (90.7%) male veterans and 5235 (9.3%) female, reflecting the gender balance of the UK Armed Forces. The earliest date of entering service was January 1960; the latest date of leaving service was December 2012. The mean period of follow-up was 29.3 years, and there was a total of 6.7 million person-years of follow-up among veterans and non-veterans combined. During the period of follow-up, 294 (0.52%) of the veterans had a diagnosis of leukaemia, Hodgkin lymphoma or non-Hodgkin lymphoma, compared with 974 (0.56%) of the non-veterans. The difference was not statistically significant, unadjusted hazard ratio (HR) 0.96, 95% confidence intervals (CI) 0.84–1.10, p = 0.541. The hazard ratio was unchanged after adjusting for areal deprivation (Table 1). Mean age at diagnosis of leukaemia was 51 years for veterans and 50 years for non-veterans. For Hodgkin lymphoma the mean age at diagnosis was 41 years for veterans and 37 years for non-veterans, whilst for non-Hodgkin lymphoma it was 48 years for veterans and 47 years for non-veterans.

3.2. Subgroup analysis

There were 125 (0.22%) cases of adult leukaemia in veterans compared with 365 (0.21%) in non-veterans. For Hodgkin lymphoma the figures were 59 (0.10%) and 182 (0.11%) respectively, whilst for non-Hodgkin lymphoma there were 144 (0.26%) cases in veterans and 538 (0.31%) in non-veterans. The Cox proportional hazard ratios showed no statistically significant differences, either in the unadjusted model or after adjusting for deprivation, adjusted HR 1.04, 95% CI 0.84–1.28, p = 0.720 for all lymphohaematopoietic malignancies analysed together. There was a small