Cancer Epidemiology 50 (2017) 92–98

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Is there a socioeconomic variation in survival from renal tumours in children and young people resident in northern England (1968–2012)?

Ugonna T. Offor, Nermine O. Basta, Peter W. James, Richard J.Q. McNally*

Institute of Health & Society, Newcastle University, Newcastle upon Tyne, NE1 4LP, UK

ARTICLE INFO

Keywords:
Socioeconomic
Epidemiology
Survival
Renal tumours
Tumour stage
Wilms tumour
Children
Young people

ABSTRACT

Background: Despite strong evidence of a social gradient in cancer survival among UK adults, studies in children and young people remain inconclusive and have not included renal tumours. This study investigated the relationship between socioeconomic status and survival from renal tumours among children and young people.

Procedure: Kaplan-Meier estimation and Cox regression were used to analyse survival for all 209 renal tumours in children and young people (0–24 years) diagnosed 1968–2012 and registered by a specialist population-based registry. Sociodemographic and clinicopathologic variables, including paternal occupation at birth, were also analysed.

Results: No significant disparity in overall renal tumour and Wilms tumour (WT) survival was observed according to paternal social class [p = 0.988 and 0.808, respectively]. The strongest predictor of survival was stage, with late stage (III–IV) disease having a 4-fold higher risk of death compared to early stage (I–II) disease [p < 0.001]. Similarly, high mortality-risk was seen for late stage WT in children aged 0–14 years (Hazard Ratio = 6.37; 95% CI = 2.60–15.59).

Conclusions: This study did not detect a significant social gradient in renal tumour survival. The identification of tumour stage as a strong predictor of survival irrespective of age, necessitates the development of appropriate public health interventions that target early diagnosis and treatment.

1. Introduction

Although survival has improved over the past four decades [1], cancer remains the leading cause of death for children (0–14 years) and young people (15–24 years) in the UK [2]. While rare in these age groups, renal tumours are an important heterogeneous group of cancers, representing 4–7% of new cases in children (0–14 years) and < 1% of cases in young people (15–24 years) [3]. For several decades renal tumours have had one of the best prognostic outcomes among childhood cancers [3]. Population-based data from Europe and North America estimate 5-year survival to be > 85% for Wilms tumour (WT) and > 80% for all renal tumours [4,5]. Although 5-year survival from childhood renal tumours in the UK has improved over the past 40 years from 60% to 90% [6], with similar findings for northern England [7], survival rates continue to lag behind those of other European countries [4]. This puts childhood renal tumours at the forefront of the UK government's National Cancer Strategy to identify modifiable prognostic factors for all childhood cancers [8]. Additionally, very few studies have attempted to estimate renal tumour survival in young people, and recent European data have shown that unlike childhood renal tumours, survival has not improved significantly in young people aged 15–24 years with renal tumours [9].

While studies have highlighted socioeconomic status (SES) as a strong predictor of survival from adult malignancies in developed countries including England [10–12], few studies have investigated the role of social deprivation in cancer survival among children and young people [13–15], with none examining renal tumours. An older study of fathers' occupations had found an unexpected association between higher paternal social class and greater chance of the child dying from a malignancy [16].

Northern England has persistently had poorer health than the rest of England and continues to experience a widening health gap [17]. Limited information is available regarding social determinants of cancer survival among children and young people resident in northern

Abbreviations: CNS, central nervous system; GP, general practitioner; ICCC-3, International Classification of Childhood Cancers Third edition; IQR, inter-quartile range; NHS, National Health Service; NRYPMDR, Northern Region Young Persons' Malignant Disease Registry; NWRT, Non-Wilms renal tumour; RVI, Royal Victoria Infirmary; SES, socioeconomic status; SIOP, International Society of Paediatric Oncology; UK, United Kingdom; UKCCSG, United Kingdom Children's Cancer Study Group; WT, Wilms tumour

* Corresponding author at: Institute of Health & Society, Newcastle University, Sir James Spence Institute, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne, NE1 4LP, UK.

E-mail address: Richard.McNally@ncl.ac.uk (R.J.Q. McNally).

http://dx.doi.org/10.1016/j.canep.2017.08.010
Received 12 May 2017; Received in revised form 11 August 2017; Accepted 16 August 2017
Available online 23 August 2017
1877-7821/

England. Findings from the few studies that have investigated this phenomenon have also tended to be contradictory. While studies using individual-level measures of SES have identified a significant association between social class and survival from childhood cancers such as leukaemia [13], those using area-level measures have been less consistent [14,18,19].

This study investigated whether survival from renal tumours in children and young people resident in northern England varied according to socioeconomic status as assessed by paternal occupation at birth.

2. Methods

The study population constituted all cases of malignant renal tumours in children (defined as ages 0–14 years) and young people (defined as aged 15–24 years), diagnosed 1968–2012 and registered on the Northern Region Young Persons' Malignant Disease Registry (NRYPMDR). The registry's study area covers the northern region of England and is located in the Newcastle upon Tyne Hospitals NHS Foundation Trust, a designated UKCCSG centre which also serves as the regional specialist centre for the treatment and management of adolescent cancers with a case ascertainment of 98% [20]. All cases are manually followed up through annual contact with responsible clinicians to determine patients' current vital status and with GPs if patients have been discharged from long-term hospital clinics. This has resulted in < 1% of cases being lost to follow up [7]. Malignancies in the registry are grouped according to the International Classification of Childhood Cancers, Third edition (ICCC-3) [9].

Demographic information (age at diagnosis, gender) and details of diagnosis (year of diagnosis, tumour stage, histological subtype), are documented by the registry. Whenever possible, a copy of the birth certificate − which records paternal occupation − is also obtained.

Paternal occupation − a reliable proxy measure of SES [13,21] − was coded using the revised 1990 Standard Occupational Classification and used to assign paternal social class at the time of the study participant's birth, classified as: I − Professional; II − Managerial; IIIN − Skilled non-manual; IIIM − Skilled manual; IV − Semi-skilled; V- unskilled. Class I was considered to be the most affluent and class V the most deprived. To enable ease of analysis and comparison with other similar studies, these social classes were collapsed into the following 3 categories: Class I/II − Professional/Managerial; Class IIIN/M − Skilled non-manual/manual; Class IV/V − Semi-skilled/unskilled. A subset of study cases without documented paternal occupation or for whom no appropriate social class could be coded was created. Renal tumours were classified according to histological subtype based on ICCC-3 and further collapsed into 2 categories: Wilms Tumours (WT) and Non-Wilms renal tumours (NWRTs). Age at diagnosis was categorized as: 0–1, 2–4, 5–14 and 15–24 and year of diagnosis for all renal tumours was classified as 1968–1977, 1978–1987, 1988–1997, 1998–2007 and 2008–2012, with further analysis for WT cases according to clinical trial dates. The trial dates used for WT cases aged 0–14 years were based on clinical trials open in the UK during our study period [22–27]. The trial periods followed were: 1968–1979 (MRC-1 and MRC-2 trials), 1980–2001 (UKW1, UKW2 and UKW3 were grouped together due to small numbers and overlapping dates), and 2002–2012 (SIOP WT trial). Registry information on tumour stage is routinely obtained from histopathology reports and/or consultant notes and was categorized as early stage disease (stage I–II), late stage disease (stage III–IV), and bilateral disease for WT based on current SIOP/UKCCG staging criteria [3]. The most recent estimate for central re-examination of biopsy specimens is noted to be 78% [20].

2.1. Statistical analysis

All study covariates were treated as categorical variables, except age and year of diagnosis, which were also considered as continuous variables. Mann Whitney and Kruskal Wallis tests were used respectively to investigate the differences in median age at diagnosis between the sexes and across calendar periods, while Chi-square test was used to analyse associations between SES and covariates. Survival time was calculated as time in years from date of diagnosis to death from any cause or the last day of availability of survival information in the NRYPMDR. Study cases who were still alive were right censored from 31 December 2015. The Kaplan-Meier method was used to estimate one-, five- and ten-year survival rates according to the covariates and survival differences between groups tested via the log-rank method. Hazard ratios (HRs) with 95% confidence intervals (CI) were obtained using the univariate Cox proportional hazards to assess effect of individual covariates on survival.

Multivariate Cox regression was used to examine effect of social class on survival while controlling for potential confounding from demographic and clinicopathologic factors. Due to the relatively few cases of NWRTs, bilateral WT and young people (15–24 years) with renal malignancies within the study population, these parameters were excluded from the final Cox modelling and instead a subgroup survival analysis of all children (0–14 years) with WT was performed using multivariate Cox regression to adjust for relevant clinical and epidemiological covariates. Interactions were tested within the Cox regression framework. The likelihood ratio test was used in the assessment of nesting effects. A significance level of 0.05 was chosen for all tests. The Schoenfeld residuals were used to investigate the validity of the proportional hazards assumption for the Cox regression models and the global score test of proportional hazards based on the scaled Schoenfeld residual was used for all significant covariates. All analyses were performed using STATA version 14.0.

3. Results

3.1. Descriptive characteristics of study population

209 renal tumours were diagnosed during the study period. The sociodemographic and clinicopathologic characteristics of the study population are summarized in Table 1. Children with WT accounted for 78% of the study population and over 70% of cases were diagnosed before 5 years of age with children aged 2–4 years constituting the modal age group while less than 10% of tumours occurred in young people (Table 1). Age at diagnosis ranged from 0 to 24 years, with a median age of 3 years and interquartile range (IQR) of 5 years. There was no significant sex difference in age at diagnosis ($p = 0.998$).

The study population consisted of 116 females and 93 males. While this sex distribution was maintained for children aged 0–14 years (male: female = 0.8), the proportion of males was slightly higher than females among young people aged 15–24 years (male: female = 1.1). Information on paternal social class was available for 183 cases. The modal social class was IIIn/m and there was no association between SES and tumour stage ($p = 0.502$) or histological subtype ($p = 0.958$).

WT was the most commonly diagnosed renal tumour (85% of cases) (Table 1). This was similar across all diagnostic periods, during which there was no significant change in the proportion of WT and NWRTs cases ($p = 0.267$). A higher proportion of WT and NWRTs cases were noted to present with early stage tumours than with late stage disease (53% vs 47% and 80% vs 20% respectively, $p = 0.019$). WT was mostly diagnosed before age 15 years − accounting for 162 cases with a median age at diagnosis of 3 years (IQR = 3 years). Conversely, the majority of NWRTs were seen in young people (55% of cases) with a median age of 18 years (IQR = 19 years). Overall, diagnosis with NWRTs was predominantly among males (male: female = 1.1), becoming more noticeable in young people (male: female = 1.4). By contrast, children diagnosed with NWRTs or WT were mostly female (male: female = 0.8). Of the 209 study cases, 59 had died by the end of the follow up period (Table 1).