Comorbidity trajectories in working age cancer survivors: A national study of Swedish men

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ABSTRACT

Background: A large proportion of cancer survivors are of working age, and maintaining health is of interest both for their working and private life. However, patterns and determinants of comorbidity over time among adult cancer survivors are incompletely described. We aimed to identify distinct comorbidity trajectories and their potential determinants.
Methods: In a cohort study of Swedish men born between 1952 and 1956, men diagnosed with cancer between 2000 and 2003 (n = 878) were matched with cancer-free men (n = 4340) and followed over five years after their first year of survival. Comorbid diseases were identified using hospital diagnoses and included in the analysis using group-based trajectory modelling. The association of socioeconomic and developmental characteristics were assessed using multinomial logit models.
Results: Four distinct comorbidity trajectories were identified. As many as 84% of cancer survivors remained at very low levels of comorbidity, and the distribution of trajectories was similar among the cancer survivors and the cancer-free men. Increases in comorbidity were seen among those who had comorbid disease at baseline and among those with poor summary disease scores in adolescence. Socioeconomic characteristics and physical, cognitive and psychological function were associated with types of trajectory in unadjusted models but did not retain independent relationships with them after simultaneous adjustment.
Conclusions: Among working-age male cancer survivors, the majority remained free or had very low levels of comorbidity. Those with poorer health in adolescence and pre-existing comorbid diseases at cancer diagnosis may, however, benefit from follow-up to prevent further increases in comorbidity.

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1. Introduction

Approximately 40% of cancer diagnoses are made in individuals of working age [1], and health after surviving cancer is a concern for both work and private life. Cancer and cancer treatments can have a substantial physical and psychological impact that may persist over time [2,3]. This may include increased risks for hypothyroidism, osteoporosis, diabetes, cardiovascular diseases and problems of cognitive dysfunction, pulmonary, urinary and bowel function [4–8]. However, studies monitoring long-term comorbidity have often focused on presence or absence of specific diseases [9] or treatments [10], but not on the accumulation of disease. Also, previous studies have examined on specific cancer types, such as testicular and breast cancer among adults [8], or childhood cancer survivors [11–13] for whom chronic disease risk is different from adult-onset cancer. Patients with more serious illness may be underrepresented due to loss to follow-up in surveys [14]. Little is known about heterogeneity in comorbidity trajectory, i.e. whether there may be distinct subgroups that follow different courses of disease accumulation after surviving adult-onset cancer. There is a social gradient in the risk of cancer in general [15], so socioeconomic characteristics may also increase the risk of health problems following cancer treatment particularly for more disadvantaged individuals. On the other hand, higher physical, cognitive and psychological capacity may buffer some of the disease risk [16–19]. Characterising types and predictors of

comorbidity trajectories may help to identify individuals at high risk of an unfavourable prognosis.

The aim of this study is first to identify and compare trajectories for accumulation of comorbidity over five years in working-age cancer survivors and cancer-free individuals. A secondary aim is to examine whether individual socioeconomic and developmental characteristics (physical, cognitive and psychological function) predict trajectory membership, as these factors have been found to influence cancer risk [15] and comorbidity [20].

2. Materials and methods

Using Swedish registers, data from a cohort of men born from 1952 to 1956 was analysed using group-based trajectory modelling and multinomial regression analysis. A first lifetime cancer diagnosis was identified between 2000 and 2003, and follow-up started one year after cancer diagnosis and ended at five years, death or emigration, whichever occurred first.

2.1. Cancer diagnosis

The *Cancer Register,* with a recorded high completeness [21], holds information of all cancer diagnoses in Sweden since 1958, coded according to the International Classification of Diseases [ICD]-7. To reduce the heterogeneity in cancer type, treatment and prognosis, we focused on colorectal (ICD-7 *153, 154*), male genitourinary system (including kidney and urinary tract) (*177–181*), skin (*190–191*) and lung cancers (including bronchus) (*162–163*), as well as leukaemia (*204–207 excluding 204.1*), and thyroid cancer (*194*). These diagnoses were chosen as they are relatively common. The five-year survival rate varied, with approximately 90% survival for skin, thyroid and male genital system cancers, around 60–80% for cancers of the kidney, urinary system, colon, rectum and leukaemia, and fewer than 20% for lung cancer [22,23]. Lung, leukaemia and thyroid cancers were combined due to data scarcity.

2.2. Comorbidity

Common comorbidities including depression, anxiety, osteoporosis and infectious disease [5,6,8,24] were identified using the Patient Register. We also included diseases used for the Charlson comorbidity index – myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, chronic renal failure, mild liver disease, diabetes with and without chronic complication, renal disease, hemiplegia or paraplegia, moderate or severe liver disease, and acquired immunodeficiency syndrome (AIDS/HIV) [25–28]. The Swedish versions of ICD-9 and 10 were used to identify comorbidities (codes are shown in appendix). Comorbidity at the start of follow-up was the summary of incident primary diagnoses recorded in the Patient Register (from 1987 for inpatient diagnoses and from 2001 for outpatient diagnoses). Follow-up was limited to five years as the patient register data were available up to the end of 2009. During follow-up, comorbidity was summarised every three months; for example, an incident diagnosis of one of the diseases increased the comorbidity count by one. The count is carried forward until another incident disease is identified [29,30]. As we focused on chronic conditions diagnoses viewed as acute events, such as peptic ulcer and infectious disease [30], were not carried forward.

2.3. Developmental and socioeconomic characteristics

Emotional regulation [31] and physical activity patterns [32] that have developed by late adolescence may persist into adult life; and cognitive ability in childhood correlates with mid-life cognition, socioeconomic position and behaviour [33,34]. Thus, physical, cognitive and psychological function and health characteristics in adolescence may have profound implications for future health. These measures were assessed in the conscription examination in the early 1970s when most of these men were 18–19 years of age. Trained psychologists produced ratings for psychological and cognitive function by combining evaluations using questionnaires, interviews and tests [35]. A normally distributed nine-level scale for stress resilience was constructed as a compound variable derived by combining evaluations of psychological dimensions such as social maturity, level and direction of interests, psychological energy and emotional stability [16]. Similarly, a normally distributed nine-level scale for cognitive function summarised the examination of linguistic understanding, spatial recognition, general knowledge and the ability to follow mechanical instructions. Physical function was assessed using an electronically braked bicycle ergometer with gradually increasing load. These variables were used as continuous measures with higher values indicating lower function. The disease score summarised medical examination and record review results and consisted of 0–9 categories, and this was collapsed into: 0 = no diagnosis, 1 = no serious health problems and 2 = fairly significant to significant health problems.

The Longitudinal Integration Database for Health Insurance and Labour Market Studies [36] in 1990 provided the most recent information on socioeconomic measures before cancer diagnosis. Individual disposable income after subtracting taxes [37] was used as an indicator of socioeconomic position (hereafter, it is expressed as income). It was divided into ten equally sized groups by decile points from the highest (=0) to the lowest (=9) and used as a continuous variable. Marital status was categorised as: married, single and divorced or widowed, and the married was the reference category. Age at cancer diagnosis [38] and cancer type [12] were included in the analysis.

2.4. Analytical sample

Among 284,257 men, 1125 were diagnosed with one of the defined cancer types as a first cancer between January 1, 2000 and December 31, 2003. We excluded those who died (n = 133), had a history of emigration (n = 32), or emigrated (n = 1) within a year after the diagnosis. Each of the remaining 959 men was matched at the time of the cancer diagnosis with five cancer-free subjects who were alive at the time of diagnosis and born in the same year. The most recent available information on county of residence (24 counties) was in 1985 and this was also used for matching [39]. Among the 4795 cancer-free men, we excluded 37 record duplicates and 16 individuals who died, emigrated or developed the incident cancer before the start of follow-up. Another 81 and 402 subjects were excluded from the survivor and cancer-free cohorts, respectively, due to missing data in relevant variables or an ill-defined summary disease score in the conscription assessment. Thus, 878 and 4340 subjects with and without cancer, respectively, were included in the analysis.

2.5. Analysis

Group-based trajectory modelling [40] identifies distinct trajectories for groups of individuals approximately following the same developmental course over time. Membership probability for all trajectory groups and individuals is calculated using maximum likelihood estimation, and subjects are assigned to a