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Journal of Cancer Policy



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

Original Research

Poor physical function, relationship problems and alcohol use are predictors of increased overall mortality in Swedish cancer patients: 27-years follow-up study in Stockholm County



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ARTICLE INFO	A B S T R A C T
Keywords: Cancer Physical function Relationship Alcohol use problem	<i>Background:</i> To study the mortality rates among cancer patients and whether these differences are associated with history of poor physical health and socio-economic situation. <i>Method:</i> The relation between overall mortality and 30 questions of life-style and health was investigated in all subjects ($n = 3197$) who received a diagnosis of cancer (ICD-7 140-209) between 1969 and 1996 from the Rebus-cohort created in 1969 ($n = 32186$). <i>Results:</i> The overall mortality was increased in both men and women who received a cancer diagnose if they had reported problems with physical function at the beginning of the study. Men who received a cancer diagnose also had higher mortality due to cancer if they had relationship problems (HR = 1.23, 1.02–1.48), and alcohol use problem (HR = 1.35, 1.04–1.74) at baseline. Women who received cancer also had higher risk to die in cardiovascular diseases if they had reported physical function problem (HR = 1.97, 1.25–3.12) at the beginning of the study. <i>Conclusions:</i> Poor physical function is a predictor of increased mortality among subjects with diagnosis of cancer.

1. Introduction

According to the World Health Organization, cancer claimed 8.2 million lives worldwide in 2012 [1,2]. Studies have shown that there are differences in incidence of all types of cancer between men and women [3,4]. According to WHO the 5 most common sites of cancer in men are: lung, prostate, colorectum, stomach and liver cancer. In women are breast, colorectum, lung, cervix and stomach cancer 5 most common sites of cancer [1,5].

An increase in age-adjusted incidence of cancer is partially explained by increased longevity [6]. In Sweden, there are 75 000 patients treated for cancer every year and according to the Swedish National Board of Health and Welfare, approximately one in three will get cancer during his/her lifetime. In 2007 alone, fifty thousand diagnoses of cancer were registered in Sweden and 22 631 persons died of cancer [7]. The most common cancer type in men in Sweden is prostate cancer (17.7% of all cancer cases) and in women breast cancer (14.1% of all

cancer cases).The age adjusted incidence of cancer does not differ between men and women [7].

Between 1982–2002, cancer mortality rates within the European Union decreased by 7% [8]. In Spain the overall mortality rate declined by 1% a year in both men and women between 1995 and 2004 [8]. That decreasing trend was thought to be the result of lowered tobacco consumption which caused cancers up to 3.72% in men and 3.77% in women [8]. A similar pattern was observed for Italy between 1970 and 2007 where total mortality rates in men declined by 1.8% and in women by 1.1% [9]. A reduction in tobacco and alcohol consumption and improved diagnosis and treatment of breast and cervical cancers where thought to be the reasons for the decline in cancer mortality rates in men and women, respectively [9].

A large Swedish study with over 2 million participants showed differences in mortality between men and women and a significant association between socio-economic status and mortality due to cancer among others [10]. Specifically, socio-economic status was strongly

https://doi.org/10.1016/j.jcpo.2018.04.003 Received 26 December 2017; Accepted 9 April 2018

Available online 20 April 2018

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Abbreviations: HR, hazard ratio; CI, confidence interval; MR, mortality rate

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associated with mortality from breast cancer in women, i.e. increased mortality from breast cancer was observed in those with a high socioeconomic status. A study from New Zealand showed that the contribution of cancer to inequalities in mortality by income has been greater than that of cardiovascular disease in women in the 1980s [11].

Furthermore, a population-based study of patients with lung cancer showed that women with low education and early stage lung cancer had poor survival odds due to co-morbidity or lifestyle factors [12].

In patients with gastrointestinal stomach tumour survival is lower in patients younger than 50 years regardless gender and tumour size [13]. A Swedish study in men with breast cancer concluded that survival rates improved with median survival times 3.9, 4.8 and 7.2 years for men diagnosed in 1960-64, 1965-69 and 1970-74 respectively which is similar to survival trend in women with the same cancer [14]. In Italy total cancer mortality rates in males increased in all age groups and particular in older males while in women decreased in younger than 65 years old during 1955-1978 [15]. La Vecchia explained by improvement of death certification and better diagnostic routines. Similar conclusions are drawn in 2000 century and the fact of early determination is added as increasing of number of survivals. Despite of advanced medical treatment of breast cancer in women and earlier discovery of disease, survival is depending on stage of developed disease. An investigation of the overall 5 years survival of breast cancer in Thai women showed different rates of survivals in various stages of diagnosis: 100% in stage I, 85% - in stage II, 39% - in stage III and 9% in stage IV respectively [16].

More leisure time and more total physical activity were strongly associated to lower cancer mortality in a large follow-up cohort study of 4672 men and women [17]. According to the authors of this study all domains of physical activity (work, household, leisure time and transportation) and more total activity reduced the risks of mortality. However, there is a lack of studies on history of physical and psychological health before cancer diagnosis and its relationship to mortality in cancer. This study was approaching such data.

The aim of present study was to study the association between lifestyle and health issues assessed via a questionnaire and the mortality rate among cancer patients.

2. Material and methods

Data from the Rebus cohort was used in the present study. This cohort was created in 1969 via a semi-randomized sample (n = 32186), with age-dependent sampling in a ratio 3:2:1 in age-groups 18–25, 26–45 and 46–65 years of age, from the population in Stockholm county (n = 445000) (Table 2). All subjects of this cohort received a postal questionnaire during 1969 and 1970 (Table 1). The response rate was 87%. Explanatory factor analysis using polycornic correlation matrix of data was used to find a relevant clinical grouping of the 28 out of 30 questions (Table 1) (results are not shown). (Two items were excluded in this context because of too much missing data (Item-2 and Item-21) in Table 1).

A follow-up of diagnoses of cancer (ICD-7 140-209) was made in 1996 from three registers: National Cause of Death Register (1996), National Register of Patients (1974) and National Cancer Register (1950–1996). From 1969 to 1996 3197 cases of primary diagnosis of cancer were found in this cohort. The initial Rebus study from 1969 was made without ethical application but the follow-up in 1996 was proceeded by two ethical applications with approval from the Regional Ethical Committee of the Karolinska Institutet (No 76/1993 and No 362/1995).

The predictive value of answers in the questionnaire 1969, comprising 28 questions of life style and health (Table 1), concerning overall mortality in subjects who had received a diagnosis of cancer between 1969 and 1996 (n = 3197) in the Rebus cohort (n = 32186) was investigated in the present study. The results of the previously performed explanatory factor analysis were confirmed by confirmatory

Table 1

27 of total 30 questions and 7 dimensions (result of after explanatory factor analyses).

Physical health problems

- 1. Do you have problems with daily activities because of physical complaints?
- 2. Do you feel sick and unwell?
- 3. Do you have any diseases or longstanding complaints?
- 4. If yes, what are they?
- 5. Do you feel fatigued?
- 6. Are you troubled with dizziness?
- 7. Do you need to take medication for headaches or other pain?
- Psychological health problems

8. Do you have trouble with daily activities because of nervous complaints?

- 9. Do you need to take sedatives?
- 10. Do you need to take sleeping pills?
- 11. Have you visited the doctor for nervous complaints any time during the past 5 years?

Relationship problems

- 12. Do you have problems with daily activities because of problems at work?
- 13. Do those around you demand too much from you?
- 14. Do you have problems with anyone close to you?

Problems with physical function

- 15. Are you handicapped?
- 16. Do you have difficulty climbing stairs?
- 17. Do you have difficulty walking indoors?
- 18. Have you been treated at the hospital for longer than a month any time during the past 5 years?

Socioeconomic problems

19. Do you have housing problems?

20. Do you have difficulties making ends meet? (i.e. serious difficulties with personal finances)?

21. Have you received social welfare payments any time during the past 5 years?

- 22. Have you been involuntarily unemployed at any time during the past 5 years?
- Depressive problems

23. Does the future look bleak to you?

- 24. Do you usually feel discouraged when you compare yourself to others?
- Alcohol use problem
- 25. Do you use alcohol?
- 26. Do you drink at least half bottle of spirits or two bottles of wine each week?

27. Has alcohol become a problem for you?

factor analysis (RMSR = 0.0776, SRMSR = 0.0776, GFI = 0.9593, AGFI = 0.9484, Parsimonious GFI = 0.8176, Bentler-Bonett NFI = 0.9457). The explanatory factor analysis used a correlation matrix based on nonparametric methods, and then oblique rotation was chosen to optimize the estimation of factor loadings.

Cox regression with the option exact ties method was performed to analyze the relation between the answers of the questionnaire (Table 1) and overall mortality (Table 3). Adjustment was made for possible confounders: age, gender and year of diagnosis. Results from survival analysis are presented with the HR and 95% confidence intervals. The reanalysis of the Rebus cohort data was approved by the Regional Ethical Committee of the <u>Karolinska Institutet</u> (2010/5:11, 2015/648-31).

3. Results

A total of 3197 persons with cancer diagnosis were included in the study (men n = 1246 (61%), women n = 1951 (39%)). Mean age of diagnosed cancer in women was 37.35 (SD 13.70) and 45.65 (SD 12.16) in men. Thus, women were younger at age of first diagnosis of cancer than men. A total number of non-survivals in 1996 was 1533 (men n = 826 and women n = 707) (Table 2). The prevalence of women living with cancer in 1996 was twice higher than the prevalence of men in the cohort, but without correction for the age difference. Sixty four (64%) percent of women lived in 1996, while only thirty four (34%) percent of men (Table 2).

Fig. 1 presents differences in cumulative proportion surviving among men and women over time (days) for 1969–1996 for all cases of death (Fig. 1A), death in cancer (Fig. 1B), death in cardiovascular diseases (Fig. 1C) and finally for death in other medical conditions

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