RESEARCH ARTICLE

Perceived Physical Strain at Work and Incidence of Prostate Cancer – a Case-Control Study in Sweden and Finland

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Abstract

   The evidence that prostate cancer is associated to physical inactivity is inconsistent. We studied the association of perceived physical workload (PPWL) at work and incidence of prostate cancer in a case-control setting. We used data from the Nordic Occupational Cancer study from Finland and Sweden. Five population controls were selected for each prostate cancer patient, matched on age and country. We had 239,835 cases and 1,199,175 controls in our study. For each case and control we estimated cumulative PPWL based on probability, level and duration of PPWL using the NOCCA Job Exposure Matrix. We then stratified individuals as having no exposure (reference category), low physical activity (below 50th percentile of the exposed), moderate exposure (50th-90th percentile) and high exposure (90th percentile and higher). The hazard ratios for prostate cancer from the lowest to highest cumulative PPWL levels were 0.90 (95% confidence interval 0.89-0.91), 0.88 (0.87-0.89) and 0.93 (0.92-0.95). There was no statistically significant dose response effect of PPWL on prostate cancer incidence. Inclusion of socioeconomic status in the model did not substantially change the result. The results were similar before Prostate Specific Antigen (PSA) testing and during the years of PSA testing in these countries. In summary, individuals with physical strain at work had a lower risk of invasive prostate cancer as compared to individuals without physical strain at work.

Keywords: Epidemiology- invasive prostate cancer- physical workload

Introduction

   Prostate cancer (PC) is the most common cancer in older men in the western world (Wong et al., 2016). Incidence rates increased steadily from the beginning of 1970's to the end of 1980's (Jemal et al., 2003). After the introduction of prostate specific antigen (PSA) testing in the late 1980's PC incidence rates have soared, due to detection of asymptomatic early state PCs (Potosky et al., 1995). Some of the PCs detected in PSA test are of low risk of progression, and can safely be followed-up clinically without active treatment for years, and may still later be treated surgically or with radiation therapy if PC becomes more aggressive (Herden et al., 2016). Despite this PC mortality rates in the developed countries have stayed quite constant over the years.

   Physical activity (PA) is one of the most important lifestyle factors that may reduce the risk of several cancer forms (Leitzmann et al., 2015). Reduced risk of prostate cancer has been reported in the Nordic Occupational

Cancer (NOCCA) study in professions that require continuous physical activity, i.e., gardeners, fishermen, forestry workers, miners and quarry workers, smelting workers as well as several others (Pukkala et al., 2009). In a recently published study it was noted that early onset-PC (men diagnosed before the age of 50) was most common in public safety workers and military personnel (Barry et al., 2017). The reasons behind this finding require further research.

   In a meta-analysis published in 2012, an inverse linear association was noted between localized PC and body mass index (BMI, defined as weight in kg/ height in meters squared), while f or advanced PC there was a linear positive association with BMI (Discacciati et al., 2012). It has been postulated that BMI might not be an ideal marker of body composition, especially for PC studies, as the positive association seen in some studies between BMI and PC incidence could be caused by lean body mass or muscle mass, which are associated with increased circulating androgen levels (Severson et al., 1988).

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Socioeconomic status (SES) seems to predict active PSA-screening (Burns et al., 2012). In a Norwegian cohort study the incidence of PC, probably due to increased PSA-testing, was elevated among men of high SES when compared to low SES (RR = 1.30; 95% CI 1.05-1.61). Men who were highly educated had similarly an increased risk for PC-diagnosis when compared to those with least education (RR = 1.56; 95% CI 1.11-2.19). In the same study a 20-percent protective effect was detected with leisure-time physical activity (RR = 0.80; 95% CI 0.62-1.03 for high vs low activity) (Lund Nilsen et al., 2000). In another study SES was studied in relation to cancers of male genital organs in Finnish men aged 45-69 years of age between years 1971-95. The incidence of prostate cancer was 40-50% higher in men of the highest SES than men of the lowest SES. The difference diminished significantly in the 1990s (Pukkala and Weiderpass, 2002).

The aim of this study is to assess effect of perceived physical workload (PPWL) at work and the incidence of invasive prostate cancer in Finland and Sweden.

Materials and Methods

We used a nested case-control design within the Nordic Occupational Cancer Study (NOCCA) cohort. This cohort consists of 14.9 million people from Nordic Countries (Finland, Iceland, Norway, Denmark, and Sweden) who participated in population censuses in 1960, 1970, 1980/1981, and/or 1990. A detailed description of the NOCCA cohort has been given by Pukkala et al., (2009). As we did not have access to the individual records neither of the Danish nor the Norwegian parts of the cohort, their data were not included. Occupational histories of individuals from Iceland were not available for us, thus these data were not included.

Occupational data was obtained from digital census records from 1960 and later censuses in Sweden and from 1970 and later censuses in Finland. Unique personal identity codes were used for linking the records from census with cancer registry data and national population registries for information on death, and emigration from the country (Pukkala et al., 2009).

The cancer registries in Finland and Sweden have collected information on almost every single cancer case diagnosed since the 1950s, and their data is of high quality (Pukkala et al., 2017).

For this study all incident prostate cancer cases diagnosed between the first available census and the 31st of December 2005 were extracted from the NOCCA cohort. Five controls for each cancer case were randomly selected among men who were alive and without a reported diagnosis of prostate cancer on the date of diagnosis of the case (hereafter the "index date" of the case–control set). Cases and controls were matched for year of birth and country. Individuals with minimum age of 20 years at index date, and having occupational information from at least one census record before the index date, were included in this study. Having a cancer diagnosis before prostate cancer incidence (for cases) or inclusion date (for controls) was not considered an exclusion criteria.

For each case and control, the PPWL was estimated based on conversion of occupational codes to quantitative amounts of PPWL with the NOCCA Job Exposure Matrix (JEM) (Kauppinen et al., 2009).

The PPWL is characterized by probability (P) and average PPWL (L). The unit of exposure was defined as a score of workers reporting heavy or rather heavy physical work in a national interview survey, which was conducted in 1990 as a part of the national 'Quality of Work Life Survey' in Finland. ("Content Areas of Quality of Work Life Surveys" 1990). When most workers in an occupational category reported very heavy workload in their profession, the value approaches one. If most respondent reported only fairly heavy work, the value approaches zero. If <10% persons in the occupation reported heavy or rather heavy physical work, the PPWL was set to zero. The estimated PPWL was highest among reinforced concrete layers, stonemasons, and concrete shutters (Annex Table 1).

We quantified the cumulative exposure to PPWL for all cases and controls. Physical workload of all individuals was calculated by using the time (T) between the age of 20 (typical age to start working in non-academic occupations) and the age of 65 (typical retirement age) or index date as a multiplier for the P*L-exposure of the profession of the individual (Table 1). After this, the individuals with PPWL above the baseline level, which was defined as P*L*T being zero, were divided to low (lowest 50% of the non-zero P*L*T; <7.37 PPWL-years), moderate (between 50 and 90 percentiles; 7.37-20.1 PPWL-years) and high (highest 10%; >20.1 PPWL-years) categories. If there were different occupational codes in census records for an individual, he was assumed to have changed occupations in the middle of the period between known census years.

Based on the introduction of PSA-testing at the end of 1980's, as well as the possible SES-bias in access to it, we conducted stratified analyses for the period before and after 1990 in order to evaluate the effect of PSA-testing on our main results. We used year 1990 as a cut-point because PSA-testing became widely available that time. (Oesterling et al. 1995).

Results

Altogether 239,835 PC-cases and 1,199,175 controls were identified during the study period (Table 1). The average age at diagnosis was 72.2 years. Most men were over 60 years old when they were diagnosed with PC, but there were a few cases that were diagnosed also in men under the age of 30.

The lowest risk estimate for PC was observed for moderate cumulative PPWL level; the HR was 0.88 (95% CI 0.87-0.89) when compared to the reference population. Reduced risks were also observed for low PPWL level (HR=0.90, 95% CI 0.89-0.91) and for high PPWL level (HR=0.93, 95% CI: 0.92-0.95). We observed statistically significantly decreased risk of PC, though without a clear dose-response pattern (Table 2).

After adjustment for SES the HRs were 0.94 (95% CI 0.93-0.95), 0.94 (0.92-0.95) and 0.97 (0.95-0.99) for the low, moderate and high PPWL groups (Table 2).

Table 1. Characteristics of Study Population for Prostate Cancer Data in Finland and Sweden

Characteristics	Case		Control	
	n	%	N	%
Total	239,835	100	1,199,175	100
Age at index date				
<40	22	0.0	105	0.0
40-60	20,198	8.4	101,515	8.5
60-80	175,645	73.2	877,070	73.1
>80	43,970	18.3	220,485	18.4
Country				
Finland	58,921	24.6	294,605	24.6
Sweden	180,914	75.4	904,570	75.4
Period				
Before 1990 (pre-PSA)	83,772	34.9	418,860	34.9
1990-2005 (PSA)	156,063	65.1	780,315	65.1
Socio-economic status				
Upper white-collar	59,318	24.7	257,201	21.5
Lower white-collar	83,527	34.8	424,643	35.4
Upper blue-collar	68,317	28.5	358,869	29.9
Lower blue-collar	14,102	5.9	78,631	6.6
Farmer	11,066	4.6	53,500	4.5
Economically inactive	3,503	1.5	26,331	2.2

Table 2. Hazard Ratio (HR) and 95% Confidence Interval (95% CI) for Prostate Cancer, by Cumulative PPWL Exposure in Finland and Sweden, with an without Unadjustment for Socioeconomic Status (SES)

	Unadjusted			Adjusted for SES		
Exposure	HR	95% CI	p-trend	HR	95% CI	p-trend
Cumulative PPWL[1]						
Reference	1.00	Ref.		1.00	Ref.	
Low	0.90	0.89-0.91		0.94	0.93-0.95	
Moderate	0.88	0.87-0.89		0.94	0.92-0.95	
High	0.93	0.92-0.95	<0.01	0.97	0.95-0.99	<0.01

[1], Cut-points are based on 50th and 90th percentile of exposure distribution among exposed subjects.

Table 3. Hazard Ratio (HR) and 95% Confidence Interval (95% CI) for PPWL Exposure and Prostate Cancer in Finland and Sweden Stratified by PSA-period, with and without Adjustment for Socioeconomic Status (SES)

Cumulative PPWL[1]	Case	Control	Unadjusted			Adjusted for SES		
			HR	95% CI	p-trend	HR	95% CI	p-trend
Before 1990 (pre-PSA period)								
Reference	30,205	144,069	1.00	Ref.		1.00	Ref.	
Low	22,290	114,081	0.90	0.89-0.91		0.94	0.92-0.96	
Moderate	21,980	114,294	0.88	0.87-0.89		0.94	0.92-0.96	
High	9,297	46,416	0.93	0.92-0.95	<0.01	0.99	0.95-1.02	0.01
1990 and later (PSA period)								
Reference	56,720	261,649	1.00	Ref.		1.00	Ref.	
Low	54,533	282,317	0.89	0.88-0.90		0.94	0.92-0.95	
Moderate	38,548	204,829	0.87	0.86-0.88		0.93	0.92-0.95	
High	6,262	31,520	0.92	0.89-0.95	<0.01	0.96	0.93-1.00	<0.01

[1], Cut-points are based on 50th and 90th percentile of exposure distribution among exposed subjects.

The HRs were virtually identical before and during the PSA-testing period (Table 3).

Discussion

Our study shows that the incidence of PC was lower in individuals with PPWL compared to individuals without PPWL, but there was no evidence of a dose-response relationship.

When interpreting our results, one potential limitation of the present study is exposure misclassification, which may arise from the following sources. First, the generic JEM does not take into account the variation of PPWL between individuals in the same occupation category, but an average PPWL is given to every individual in the same occupational category. NOCCA-JEM does not account for industries but only occupational groups. PPWL intensity and prevalence may vary by industry included into the same occupational group (Wang et al., 2009). Hence, a lack of information on industry may also contribute to misclassification, in the case of this study of physical strain at work, and bias the association between exposure and outcome of interest (Stewart and Herrick, 1991).

The incomplete data on work history may also contribute to exposure misclassification. People's work histories were based on census records that are merely snapshots of jobs held in the year before the time of the census. The data did not provide exact information on the changes of the job or tasks during the entire career. The census information was known from years 1960-1990, and the oldest individuals may have started their work life more than 40 years before the first known census occupation. If the person was still at rather high age in a physically demanding job, it was unlikely that he would have been in the beginning of his/her career in a physically less demanding job, while the change to physically less demanding job in older age is more common. Therefore it is likely that the persons classified to the highest PPWL category truly belonged in that category but there may be persons in the reference category with some PPWL exposure. This misclassification would bias the HR values towards unity and lead to slightly too low estimates of the protective effect in our study.

The associations between lifestyle, physical activity at work and the risk of PC reported in previously published studies have been inconsistent. Lifetime total occupational physical activity did not prove to be protective of PCs in a Swedish study published in 2008 (Wiklund et al., 2008). On the contrary, there was an increased risk of PC for men that had a high amount of physical activity in their work. There was a significantly decreased risk in high physical activity workers in the US (Krishnadasan et al., 2008) but several other studies have been inconclusive or negative (Sass-Kortsak et al., 2007). Often these results can be explained by small sample size and short follow-up.

We were unable to control for the leisure time physical activity of the subjects. However, on population level we were able to assess the effects of independent lifestyle factors to a satisfactory degree. Some studies have reported a small decrease in PC risk for increased leisure time PA (Littman et al., 2006), but recently some conflicting findings have been reported: an increased PC incidence has been reported in a meta-analysis of 12 different studies from US and Europe comprising of 1.44 million adults. Intense leisure-time physical activity was associated with a 5% increased risk of prostate cancer (HR, 1.05; 95% CI, 1.03-1.08) (Moore et al., 2016).

Advantages of the study are important. The Nordic cancer registries (Pukkala et al., 2017) have reportedly a very high accuracy and completeness when it comes to their data. In addition to that we've had access to the accurate job history of the participants of this study (Pukkala et al., 2009) to a very satisfactory degree. The completeness and the amount of the data makes this dataset unique.

In addition to this the general lifestyle and access to healthcare for all social classes, thanks to tax funded health care, is almost identical to everyone living in Finland and Sweden. In addition to that in both countries the local municipalities support different health promoting activities e.g. cheap access to sports facilities.

Our study confirms the association between physical activity and the incidence of PC: in fact even modest levels of physical activity (PA) at work can reduce the incidence of PC significantly (Cuzick et al., 2014). In addition, the results were almost identical at the time before the era of PSA-testing and during PSA-testing. Most importantly our study adds up to the finding presented by earlier research that especially the lack of physical activity and sedentary lifestyle seem to be associated with higher risk of PC than any level of physical activity.

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