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Original Article

Occupational activity and risk of prostate cancer in Ireland

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Abstract

Study Objective: The study intended to investigate the possible relationship between physical activity and prostate cancer risk on a previously unexamined population set.

Design: A population-based study was conducted on males entered on the Irish Cancer Registry between the years 1994 to 1997 to investigate if physical activity affected the risk of prostate cancer. Activity was coded for three levels of occupational activity and the odds ratios were calculated together with 95% confidence limits.

Results: Despite limitations in the data, an elevated risk (odds ratio 2.13, 95% confidence interval 1.29–3.52) was seen in working subjects with low levels of activity compared with the high activity group. In the retired group there was a slight elevation of risk, although it was not statistically significant.

Conclusion: The study suggests that physical activity offers a small but significant reduction in prostate cancer risk for those people in work.

Keywords

Prostate cancer; cancer risk; occupational activity

INTRODUCTION

Recently governments and agencies in the UK, America and Ireland have recognised the potential importance physical activity can have on cancer risk in later life. Programmes are currently being put in place such as the action cancer road-shows to encourage physical activity in children and adults in the hope that the incidence of certain cancers, particularly colon cancer will be reduced. There is evidence from some epidemiological studies[1,2] of an inverse relationship between physical activity and the incidence of prostate cancer, although the evidence at the moment remains inconclusive, as the association is not consistent across studies. The relationship, where it is seen to exist, is comparatively weak, with most studies reporting the decreased risk for active populations as being between 10% and 70%.[3]

Prostate cancer shows a marked geographical variation in incidence between countries, being most common in western countries, particularly the United States of America, whereas the Asian and developing countries have the lowest rates.[4] In Ireland, prostate cancer is the third most common site of cancer after non-melanotic skin cancer and lung cancer, with a higher than average incidence rate for the European Union. The incidence rate, between the years 1994 to 1998, of the occurrence of tumours was shown to be significantly increased in all age groups.[5] This may, however, be as a result of augmented detection through the increased use of the prostate specific antigen (PSA) test rather than a true increase in incidence. The aetiology of prostate cancer

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remains comparatively unclear, in terms of both; genetic and environmental risk factors. The main factors[6] implied to date are:

1. Age: the disease generally being considered a disease of the elderly, the incidence rising steeply in men over 60.
2. Race: (the relative risk in the USA being higher in the Afro-Caribbean population by a factor of almost two compared with Caucasians). The incidence also seems to be dependant on adaptation of diet and lifestyle as the risk increases among Asian men who adopt a Western lifestyle.
3. Familial predisposition to prostate cancer is also a major factor, particularly in first-degree family members. The risk is additionally higher for men with a history of prostate cancer on the mother's side of the family compared to the father's side.[7]

All of these factors are considered un-modifiable and therefore unusable as a means of managing this disease.

Several biological explanations have been hypothesized to support this possible relationship. Physical exercise is known to increase the number and activity of certain white cell populations including NK cells.[8,9] This could elevate the activity of the immune system enough to increase the pick up of early malignant changes, so reducing the likelihood of a clinical cancer developing. Physical activity is also known to alter hormonal levels, suppressing serum levels of testosterone,[10] and insulin-like growth factor I (IGF-I), which have been shown to reduce growth of LNCaP prostate cells in vitro.[11] Hormone manipulation in vivo is also known to be effective for prostate cancer; low levels of androgens are protective, the disease being very rare in men castrated before puberty and treatment often revolves around initial control of the tumour by hormone therapy. It has also been suggested that physical activity may affect tumour growth indirectly by modifying body weight and the amount of fat present, which in turn may affect hormone levels and prostate cancer risk.

METHOD

The study was population-based, using data on male cancers between the years 1994 to 1997 inclusive supplied by the National Cancer Registry, Ireland. Occupation was coded according to a scheme developed by Garabrant,[12] which gave three levels of activity: sedentary (jobs requiring activity $<20\%$ of the time); moderately active (jobs requiring activity 20–80% of the time); and highly active (jobs requiring activity $>80\%$ of the time). The original coding scheme was based on the 1970 (US Bureau of Census) codes; where possible a direct transfer of the code was made to the appropriate Irish occupation. Where there was no direct comparison, a team of five individuals were asked to individually code activity based on the scoring system with the modal value being used. When complete, a third party then reviewed all the occupations and their respective activity codes.

Some subjects were excluded from the investigation due to the reasons identified in Table 1. Subjects under the age of 40 were excluded from the analysis, as the lead-time for certain tumours to development is variable and can be of long duration. Job activity was considered likely to play a negligible role in suppressing tumour development in people in a low age-bracket. As there were no prostate cancer cases in subjects below the age of 40, it was considered a suitable cut-off point for the control group, which was established using data from all other cancer cases. The adjustment for age when done was carried out using quartiles. Analysis of the data was limited to 15,737 subjects (Table 2), obtained from the Registry. This means that the data set was limited to approximately half of the original data set. The major reason for this was poor occupational reporting, particularly in the retired population. This figure is considerably higher than that reported by Garabrant[12] who reported missing data for approximately 20% of their population.

Logistic regression using SPSS® version 11.5 was used to calculate the odds ratio (OR) and 95%

Table 1. *Excluded data*

Reason	n
Unknown Occupation	12,108
Unclassifiable Occupation	2,329
Unknown Tumour site	916
Under 40 years of age	901
Total	16,254

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Table 2. Number of subjects by cancer site

Tumour site	Frequency	Percent
Prostate	3,008	19.1
Lung	2,652	16.9
Colon	1,878	11.9
Bone Marrow	941	6.0
Rectum	935	5.9
Bladder	910	5.8
Stomach	801	5.1
Others (<5%)	4,612	29.3
Total	15,737	100

Table 3. Prostate histologies

Tumour histology	Frequency	Percent
Adenocarcinoma	2,529	84.1
Unspecified	370	12.3
Unspecified carcinoma	96	3.2
Squamous cell	10	0.3
Small cell	2	0.1
Sarcoma	1	0.0
Total	3,008	100

confidence intervals (CI) of the prostate cancer incidence associated with physical activity, whilst adjusting for confounders. The cancer site with the largest amount of evidence linking it to physical activity is the colon. Studies[3,13] examining this relationship overwhelmingly show an inverse relationship between physical activity levels and risk. Although not as conclusive as the evidence for prostate and colon cancers, some research[14,15] has also indicated that lung cancer may also be related to physical activity. This evidence together with the high frequency of these tumours compared to others, subjects with colon or lung cancers resulted in the exclusion of these patients from the control group. In all cases the threshold to reject the null hypothesis was set at $P < 0.05$.

RESULTS

Preliminary analysis using the Pearson chi squared test indicated that there was a significant relationship between physical activity and prostate cancer incidence, $\chi^2 = 12.482$, $df = 2$, $p = 0.002$ although the strength of association was very weak, Cramer's $V = 0.002$. The analysis was re-run removing all histologies other than known adenocarcinoma from the prostate group. This was considered appropriate as only adenocarcinomas may respond to endocrine fluctuation, which is postulated as being a possible cause of the relationship. The breakdown of the histologies found in the patients with prostate cancer are shown in Table 3. Comparing only known adenocarcinomas of the prostate with the control population, increased the significant difference between the populations $\chi^2 = 16.839$, $df = 2$, $p < 0.001$, and the strength of the association although still small was also improved, Cramer's $V = 0.040$.

Logistic regression was then performed using an unconditional model on the data, the results of which are seen in Table 4. All results are relative to the control group, which were the group containing subjects with an activity over 80% of the time. The model was adjusted for two factors: firstly agricultural workers – as it has been suggested that this type of occupation has a higher risk of prostate cancer, probably as a result of exposure to chemicals within pesticides (Acquella *et al.* and Keller-Byrne *et al.* in Sharma-Wagner *et al.*);[16] secondly, the variable of working status was entered into the model, comparing those still in employment with those who had retired. Age was originally included in the analysis, but as the variable did not meet the condition of the Hosmer and Lemeshow's goodness-of-fit test (so indicating that there was no difference between the observed and model predicted values of the dependent) this block of the analysis was ignored.

In order to overcome this problem and look at the relationship between working status more closely, the analysis was then re-run, firstly looking at those in employment at the time of diagnosis, and at those who had retired, (lower sections of Table 4). In this instance, age adjustment was included in the model as it met test criteria.

DISCUSSION

These results demonstrate that lower levels of physical activity as recorded by occupation were positively associated with a higher risk of prostate cancer. There was an observable difference in the descriptive measure of fit as reported by Nagelkerke's R^2 measurement when looking at the relationship of activity known adenocarcinomas compared to all prostate cancer cases. One interpretation of this finding could be that physical

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Table 4. *Logistic regression analyses*

Activity group	Nagelkerke's R^2	Significance p	Exp (B) Odds ratio	95% confidence limit	
				Lower bound	Upper bound
Known adenocarcinomas					
<20% Active		0.029	1.264	1.025	1.560
20–80% Active	0.002	0.002	1.238	1.079	1.421
>80% Most active			1.000	referent	
Known adenocarcinomas adjusted for farm work and working status					
<20% Active		0.005	1.356	1.097	1.677
20–80% Active		0.005	1.226	1.063	1.412
>80% Most Active	0.024		1.000	referent	
Farming		<0.001	1.269	1.416	1.136
Working status		<0.001	1.881	1.672	2.116
Adenocarcinomas, pre retirement, age adjusted					
<20% Active		0.003	2.130	1.288	3.523
20–80% Active	0.144	0.152	1.328	0.901	1.957
>80% Most Active			1.000	referent	
Farming		0.108	1.216	0.958	1.543
Adenocarcinomas, retired, age adjusted					
<20% Active		0.144	1.198	0.940	1.526
20–80% Active	0.012	0.112	1.137	0.970	1.333
>80% Most Active			1.000	referent	
Farming		0.140	0.906	0.794	1.033

activity is reducing the incidence by hormonal influence rather than having an effect on the immune system, which would, in all probability, affect all histologies equally. However, by excluding unspecified tumours which form the largest proportion of the excluded data we could be introducing bias as a large proportion of these tumours will be adenocarcinomas in men who have had no surgery who will tend to be in the older age bracket.

The association between physical activity and all prostate cancer cases was found to be dependent on the degree of activity; with those subjects in the least active group being at a greater risk of developing the disease 36%, compared to 23% for the moderately active population. This stage of the analysis also indicates a significant relationship ($p = <0.001$) between farming and agricultural occupations, and the chance of developing prostate cancer; although it must be remembered that it was not possible to control for age in this model and when an age-adjusted model could be used looking at both pre- and post-retirement populations separately, this relationship did not exist.

Separate analysis of the subjects based on their retirement status, clearly showed a significant relationship between physical activity and those at work that does not exist in the retired population. This would imply that the protection offered by the high levels of physical activity is valid only whilst undertaking the activity, the benefits of activity being relatively short-lived once stopped and not carried over into retirement years. Although not a direct comparison, this finding is in disagreement with those of Le Marchand *et al.*[17] who found that the risk was higher in subjects over 70 than those under 70 years of age.

Methodologically, retrospective measurement of physical activity poses a number of issues regardless of method used. The method utilised, based activity on a one-off comment on occupation and did not take into account how long that job had been held or other occupations that the individual had held which could have led to a misclassification of activity. Also, the majority of subjects were elderly, which could also affect classification as there is a tendency for there to be a move to more supervisory/managerial roles with advancing experience, which is probably more obvious in lower social class jobs.

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Another potential confounder to this method is occupational status, with many subjects being retired; the data provided no information on the age at retirement. If physical activity does play a role in reducing the likelihood of developing prostate cancer, as suggested by the results, then the lead-time to the development of the tumour and length of time the protection offered by activity, also has to be taken into account – which may affect the results of the analysis.

Finally, several other potential limitations of the study need to be addressed. Several important risk factors were not assessed within the study, as the data set provided did not contain the relevant information. Length of occupational activity has already been mentioned as a possible confounder, additionally many farmers work well beyond the "established" retirement age, which could further bias the data in this age group. It must also be noted that race and family history; two of the main aetiological factors identified by Meisner[6] were not included, and their effect on the model cannot be estimated.

The paper is supportive of the concept of physical activity as a means of reducing cancer risk. It suggests that the currently being introduced Government policy of exercise promotion may play a key role to significantly reduce the risk of developing prostate cancer.

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