in particular it is not needed for the predictions in table III.

Healy and Tillett showed that the median delay in reporting from date of diagnosis was one to two months with few delays of over six months.[4] Hence to convert the predictions in tables II and III to predictions by date of diagnosis entails an insignificant adjustment corresponding to a time shift of one to two months. As at present the median survival time after diagnosis of AIDS is about one year,[19] the number of people needing care during a given year can be estimated from table II or table III by adding the entry for that year to 50% of the entry for the previous year.

The method of scaling down to local populations can be applied to any region where accurate local case data are available. If the observed number of cases is too small the predictions will be unreliable. Other local factors, such as knowledge of specific risk factors, should be taken into account.

Predictions are an essential basis for planning local services for people with AIDS. Planning can proceed only once there is an estimate of the likely size of the case load. The form that the services take will depend on the philosophy of care, including the balance between institutional and community aspects. This balance should be made explicit, and as services need to be provided by health authorities, local authorities, and voluntary organisations, they should be planned by these agencies working together.

The long incubation period of AIDS means that preventive measures have a delayed impact. The need for prevention is emphasised, however, by the size of the predicted case load, the burden of care that this implies, and the fact that the incidence will continue to rise after the end of the five year prediction period. The local significance of these factors will be clarified by the local predictions and should encourage local preventive activities. Monitoring of national and local case data will allow validation and updating of these predictions.

We thank Professor M J R Healy and Dr D R R Williams for their help.

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(Accepted 29 June 1988)

Body mass and prostatic cancer: a prospective study

Richard K Severson, John S Grove, Abraham M Y Nomura, Grant N Stemmermann

Abstract

Previous studies have suggested that increased body mass is associated with an increased risk of prostatic cancer, but these studies have been limited by the fact that they were based on a few simple measurements such as height and weight. Similar results were found in a prospective study of the incidence of prostatic cancer in a cohort of Japanese men born in 1900-19 and living in Hawaii. Further evaluation of the extensive anthropomorphic measurements made in this cohort suggested that the association between measures of body mass and prostatic cancer might be accounted for more by lean tissue than by fat tissue. There was a significant positive association of the risk of prostatic cancer with area of muscle in the arm but not with area of fat in the arm.

Further research is needed on the biological mechanisms of carcinogenesis that may be related to both lean and fat tissue and the development of prostatic cancer.

Japan-Hawaii Cancer Study, Kuakini Medical Center, Honolulu, Hawaii 96817, United States
Richard K Severson, PHD, *epidemiologist*
John S Grove, PHD, *biostatistician*
Abraham M Y Nomura, MD, *director*
Grant N Stemmermann, MD, *pathologist*

Correspondence to: Dr R K Severson, Program in Epidemiology W403, Fred Hutchinson Cancer Research Center, Seattle, WA 98104, United States.

Introduction

Although several studies have attempted to identify factors that cause prostatic cancer, little has been established. Recently it was reported that the risk of prostatic cancer increased with increasing body mass index.[1] This finding, which was derived from a hospital based case-control study of the incidence of prostatic cancer in northern Italy, is consistent with mortality data from prospective studies of Seventh Day Adventists[2] and volunteers from the American Cancer Society[3] in the United States, which both found an increased risk of prostatic cancer in overweight men. These studies were restricted in that they related risk solely to variables based on height and weight. We report a prospective study of the incidence of prostatic cancer in a cohort of Japanese men living in Hawaii in which we recorded extensive anthropomorphic measurements.

Patients and methods

A cohort of 8006 Japanese men who had been born during 1900-19 and were living in the Hawaiian island of Oahu in 1965 were examined and interviewed from 1965 to 1968.[4] Several anthropomorphic measurements were recorded during the clinical examination. Body mass index was calculated as weight (kg)/(height (m))^2, and the areas of muscle and fat in the upper arm were calculated according to the equations of Heymsfield *et al* and Frisancho, respectively.[5,6] Seven men with prostatic cancer at the time of examination were eliminated from the analysis.

The time at risk of prostatic cancer was calculated for each subject as the time from examination to a

histologically confirmed diagnosis of prostatic cancer, death, or September 1986, whichever occurred first. These calculations resulted in a total of 139 727 person years at risk. The relative risk of prostatic cancer was estimated from proportional hazards regression models, while adjusting for age at examination.[7]

Results

During the surveillance period 174 cases of prostatic cancer were recorded in the cohort. Table I shows the risk of prostatic cancer associated with various anthropomorphic measurements. Body mass index showed a positive association with risk of prostatic cancer, but the test for trend was not significant (p=0·13). To evaluate this association further the relative risk for men with a body mass index ≥28 kg/m² (those in the highest tenth) compared with men with a body mass index <20 kg/m²(those in the lowest tenth) was calculated as 2·32 (95% confidence interval 0·99 to 5·46).

TABLE I—*Relative risks (adjusted for age) and 95% confidence intervals for prostatic cancer associated with selected anthropomorphic measurements taken at first examination of Japanese men in Hawaii, 1965-86*

	No of cases	No of controls	Relative risk	Confidence intervals
Body mass index:				
0-22·49	53	2573	1·00	
22·50-24·49	57	2478	1·23	0·85 to 1·79
≥25	64	2769	1·33	0·92 to 1·92
Skinfold thickness of left triceps (mm):				
0-6	64	2832	1·00	
7-8	51	2187	1·00	0·69 to 1·44
≥9	59	2801	0·94	0·66 to 1·33
Girth of left upper arm (cm):				
0-26	47	2399	1·00	
27-29	83	3274	1·59	1·11 to 2·29
≥30	44	2151	1·49	0·98 to 2·26
Skinfold thickness under left scapula (mm):				
0-12	52	2583	1·00	
13-19	67	2719	1·34	0·93 to 1·92
≥20	55	2519	1·27	0·87 to 1·86
Biacromial diameter (cm):				
0-37	73	3065	1·00	
38-39	65	3040	1·04	0·74 to 1·45
≥40	36	1716	1·22	0·81 to 1·84
Weight (kg):				
0-58·9	55	2555	1·00	
59·0-67·9	73	2867	1·47	1·04 to 2·10
≥68·0	46	2398	1·28	0·86 to 1·90
Height when sitting (cm):				
0-85	70	2710	1·00	
86-87	48	2249	0·97	0·67 to 1·41
≥88	56	2861	0·94	0·66 to 1·34
Leg length (cm)*:				
0-74	61	2882	1·00	
75-77	54	1962	1·41	0·98 to 2·04
≥78	59	2973	1·24	0·86 to 1·79

*Height when standing minus height when sitting.

Subjects whose left upper arm had a girth of ≥27 cm had higher risks of prostatic cancer than subjects with girths of <27 cm, but the increase in risk was not linear. When age and the girth of the left upper arm were controlled for, the positive association between body mass index and prostatic cancer decreased substantially. When age and body mass index were controlled for, the risk associated with the girth of the left upper arm remained essentially unchanged.

Table II shows the risk of prostatic cancer associated with the estimated areas of muscle and fat in the arm. Risk increased significantly (p=0·026) with increasing area of muscle in the arm but was not related to the area of fat in the arm (p=0·996). The estimates of risk for subjects whose area of muscle in the arm was 4650-5549 mm² and ≥5550 mm² were similar, suggesting that the relation between the area of muscle in the arm and prostatic cancer was not linear. To examine this further the data on area of muscle in the arm were evaluated by logarithmic transformation and inverse transformation (table III). The inverse transformation

TABLE II—*Relative risks (adjusted for age) and 95% confidence intervals for prostatic cancer associated with area of muscle and fat in the arm among Japanese men in Hawaii, 1965-86*

	No of cases	No of controls	Relative risk	Confidence interval
Area of muscle in arm (mm²):				
0·4649	51	2612	1·00	
4650-5549	64	2488	1·54	1·06 to 2·23
≥5550	59	2719	1·57*	1·07 to 2·30
Area of fat in arm (mm²):				
0·799	59	2426	1·00	
800-1199	61	2876	0·88	0·61 to 1·25
≥1200	54	2517	0·96	0·66 to 1·38

*p=0·026 for increased risk of prostatic cancer with increasing area of muscle.

TABLE III—*Coefficients and standard errors (adjusted for age) for transformations of area of muscle in the arm from separate proportional hazards regression models for Japanese men in Hawaii, 1965-86*

	Coefficient	Standard error	p Value
Linear transformation	$1·67\times10^{-4}$	$7·48\times10^{-5}$	0·026
Natural logarithmic transformation	1·00	$3·97\times10^{-1}$	0·012
Inverse transformation	$-5·51\times10^{3}$	$2·01\times10^{3}$	0·006

provided the best fit (p=0·006), suggesting that the risk of prostatic cancer approaches a constant value as the area of muscle in the arm increases.

Discussion

Little is known about the cause of prostatic cancer. We found a positive association between body mass index and the incidence of prostatic cancer, which is consistent with results of previous studies. In addition, we evaluated the associations between different types of body tissue and prostatic cancer.

Both fat and lean tissue are reflected in the body mass index.[8] The area of muscle in the arm was significantly associated with an increased risk of prostatic cancer, but there was no association between the area of fat in the arm and prostatic cancer. As these two measurements are the most accurate indicators of adipose and lean body tissue[5,6] our results suggest that lean tissue rather than body fat may play a part in the development of prostatic cancer. In addition, although we consider the results presented in table III to be preliminary, they suggest that the risk of prostatic cancer increases with increasing mass of muscle only up to a certain point, after which it remains constant.

We have no firm suggestion for a biological mechanism that might explain these findings. The normal growth and functioning of the prostate are influenced by sex hormones.[9] Experimental studies suggest that testosterone has a role in starting carcinogenesis of the prostate in animals.[10] Cancer is most likely to develop in the peripheral parenchyma of the prostate, which is more dependent on androgen than is the central area.[11] Androgens (anabolic steroids) affect muscle mass and are used by athletes who wish to increase the development of their muscles.[12] Endogenous overproduction of androgens has little obvious effect in men, although it can lead to hypertrophy of skeletal muscle and virilism in women.[13] Increased muscle development in some men may perhaps reflect overproduction of sex hormones, especially hypersecretion of androgens by the adrenal cortex.[14,15] If this imbalance was maintained for long enough it might lead to an increased risk of prostatic cancer. This, however, is speculation, and further research is necessary before firm conclusions can be drawn.

We thank the following institutions for their cooperation: Castle Medical Center, Kaiser Medical Center, Queen's

Medical Center, St Francis Hospital, Straub Clinic and Hospital, Tripler Medical Center, Wahiawa General Hospital, and the Hawaii Tumor Registry. We thank Dr Marc Micozzi for helpful discussions. The study was supported by grant ROI CA 33644 awarded by the National Cancer Institute, Department of Health and Human Services, Bethesda, Maryland.

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(Accepted 10 May 1988)

Prolonged pregnancy: the management debate

In 1986 we published a paper on the management of prolonged pregnancy by Ms Cardozo and her colleagues (25 October 1986, p 1059). Drs Lang and Lieberman wrote to us suggesting an additional analysis of the data, to which Mr Pearce and Ms Cardozo responded. We here publish the details and results of this supplementary analysis.

Suggested supplemental analysis

Janet Lang, Ellice Lieberman

The study by Cardozo *et al* was the largest randomised clinical trial to date designed to evaluate strategies for managing prolonged pregnancy. In the study 402 women were randomised either to have their labour induced two to four days later (active group; n=195) or to have their pregnancy observed without any intervention, unless intervention was medically indicated (conservative group; n=207). For the active group the time between assignment to the group and induction of labour was no doubt necessary to allow the women time to make necessary practical arrangements. During this time, of course, spontaneous labour could occur; for 49 women (25%) in the active group it did, and another 21 women (11%) refused to undergo the treatment assigned to them and were therefore not induced at the scheduled time. Thus only 125 of the 195 women (64%) assigned to the active group actually had their labour induced.

The analysis performed by Cardoza *et al* was classical —that is, by intention-to-treat. Because of the relatively high levels of non-compliance with assigned treatment, however, we suggest a supplemental analysis. The first step would be an attempt to adjust for differences between the group assignment and the treatment received that resulted from the necessary two to four day waiting period between randomisation and planned induction. The critical feature of this approach (figure) is to apply the constraint of completing the two to four days' waiting time to both groups before assessing outcomes relevant to the study. During this waiting time spontaneous labour may begin, labour may be induced for medical reasons, or women may refuse the treatment assigned to them. The expectation, of course, is that the prevalence of spontaneous labour and medically required inductions would be quite comparable across the two groups. All the women in the active group who completed the waiting period will thus have had their labour induced. Of those randomised to the conservative group, the subgroup for analysis will, quite appropriately, contain women who began labour spontaneously after the waiting time; women who were induced after the waiting time because of complications; and women who requested induction after the waiting time. The second step would be to compare these two subgroups. This comparison would *not* be a randomised comparison. Thus, analytical techniques for observational studies (such as multivariate analyses) must be used so that appropriate attention is given to the control of confounding in the crude comparison of the two groups. Otherwise, the effects of bias might well contribute to the observed effects.

Departments of Medicine and Obstetrics and Gynaecology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, United States
Janet Lang, PHD, *associate epidemiologist*
Ellice Lieberman, MD *instructor, obstetrics and gynaecology*

Department of Obstetrics and Gynaecology, St George's Hospital Medical School, London SW17 0RE
J Malcolm Pearce, MRCOG, *senior lecturer*

Department of Obstetrics and Gynaecology, King's College Hospital, London SE5
Linda Cardozo, MRCOG, *consultant*

Results

J Malcolm Pearce, Linda Cardozo

We thank Drs Lang and Lieberman for suggesting the interesting supplementary analysis to our paper on the management of prolonged pregnancy. The waiting time was introduced into our trial not only to allow women to make appropriate arrangements but also to overcome the problem of intervening weekends. After performing the suggested analysis we found that 70 women (36%) in the active group went into spontaneous labour during the waiting time compared with 41 women (20%) in the conservative group. This difference was significant ($\chi^2=12{\cdot}2$, $p<0{\cdot}001$) and our only explanation for this difference is that it may have been a result of the vaginal examination performed to assess the cervix before planned induction. This examination may not have been performed on the women in the conservative group, but unfortunately we cannot verify this. An additional 10 women from the conservative group required induction during the waiting time (three for hypertension, two because of worrying results from cardiotocography, two for premature rupture of the membranes, and three because they requested induction of labour).

This left 125 women in the active group, who all had their labour induced after completing the waiting time, and 156 women in the conservative group. As in our original analysis, the conservative group contained significantly more white women ($p<0{\cdot}02$), but the groups were otherwise well matched (table I). At the onset of labour, however, significantly more fetal heads