

Null Results in Brief

Lack of Association of Physical Activity and Obesity with Incident Pancreatic Cancer in Elderly Women

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Introduction

Pancreatic cancer is relatively uncommon in the United States, but it is rapidly fatal with <5% of cases surviving 5 years (1). Little is known about its etiology; cigarette smoking is the only modifiable risk factor consistently linked to pancreatic cancer (2).

Animal models have suggested that insulin and insulin resistance may play roles in the etiology of pancreatic cancer (3, 4) and epidemiologic studies have shown an association between diabetes mellitus and increased risk of pancreatic cancer (5-7). Obesity, measured by body mass index (BMI) and waist-to-hip ratio (WHR), and physical activity can play roles in both insulin resistance and type II diabetes (8, 9).

Two recent prospective studies have examined pancreatic cancer incidence in relation to obesity and physical activity: Michaud et al. reported that individuals with a high BMI or low level of moderate physical activity were at an increased risk of pancreatic cancer (10), whereas Lee et al. reported that BMI and physical activity were not associated with pancreatic cancer risk (11). The Iowa Women's Health Study was used to analyze the association of obesity and physical activity with pancreatic cancer risk in older women.

Materials and Methods

As described elsewhere (12, 13) in January 1986, the Iowa Women's Health Study mailed questionnaires to nearly 100,000 randomly selected women ages 55 to 69 years, who had a valid Iowa driver's license in 1985. The 41,836 (42%) women who returned questionnaires were subsequently followed for mortality and cancer incidence. The University of Minnesota's Institutional Review Board approved this research study.

Vital status was obtained through follow-up questionnaires in 1987, 1989, 1992, and 1997 and through the National Death Index. New pancreatic cancers (*International Classification of Diseases for Oncology Second Edition* code C25) were ascertained through the Iowa Cancer Registry, which is part of the national Surveillance, Epidemiology, End Results program. Subjects with a history of cancer other than nonmelanoma skin cancer at baseline were excluded ($n = 3830$). Pancreatic cancer cases

determined to be islet cell carcinomas ($n = 1$), neuroendocrine carcinomas ($n = 1$), and leiomyosarcomas ($n = 2$) were also excluded. After these exclusions, 38,002 participants at risk, including 209 who developed pancreatic cancer through December 31, 2001, were included in this analysis. A sensitivity analysis was done to exclude participants diagnosed with pancreatic cancer before January 1, 1988 ($n = 14$). Results did not differ for the sensitivity analysis and therefore these cases of pancreatic cancer were included.

Methods of collection for physical activity, BMI at age 18, 30, 40, 50, and at baseline, and WHR, have been published elsewhere (12-14). Measures of baseline weight, height, and waist and hip circumferences were generally accurate and reliable (14). Participants were asked three questions about whether they participated in leisure time exercise and, if so, the frequency of moderate and heavy activities. The latter two questions were combined to create a three-level activity score.

Baseline characteristics were compared among participants who developed pancreatic cancer and those who did not using Pearson's χ^2 test or the t test. Age-adjusted and multivariate-adjusted hazard ratios (HR) and 95% confidence intervals (95% CI) were computed using proportional hazards regression. Besides study variables mentioned previously, potential confounders that showed an association with both pancreatic cancer and the study variables ($P < 0.10$) were included in the multivariate models. These confounders included age, smoking status, and multivitamin use. All statistical analyses were done using SAS 8 software (15).

Results

Compared with women who remained free of pancreatic cancer, women who developed pancreatic cancer were 0.8 years older ($P = 0.01$), two thirds more likely to be smokers ($P = 0.002$), twice as likely to have diabetes ($P = 0.0006$), and less likely to be taking a multivitamin daily ($P = 0.02$; Table 1). There were no differences between groups in mean BMI, WHR, or physical activity measures.

Age- and multivariate-adjusted pancreatic cancer incidence was not associated with any obesity category (Table 2). Women with a BMI ≥ 30 kg/m² at baseline had a HR of 1.14 (95% CI, 0.81-1.62) compared with a BMI < 25 kg/m². Women in the highest tertile of WHR had a HR of 1.12 (95% CI, 0.81-1.55) compared with the lowest WHR tertile. Multivariate-adjusted pancreatic cancer incidence also was not associated with obesity based on self-recalled weights at age 18, 30, or 50, although obesity at age 40 unexpectedly carried a pancreatic cancer HR of 1.72 (95% CI, 1.12-2.63; results not shown).

There was no association between physical activity and pancreatic cancer (Table 2). Women with a high versus low

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activity level at baseline had a HR of 1.29 (95% CI, 0.93-1.77). Finally, there was no association between body size and physical activity categories, considered jointly, and pancreatic cancer incidence (results not shown).

Discussion

This large cohort study of elderly women provides evidence that physical inactivity and obesity are not risk factors for pancreatic cancer. With our sample size, we had 85% power to detect a HR of ≥ 1.5 . Limitations of our study were a short

physical activity instrument, although one that does relate to CHD mortality (12), and single measures of exposure.

Recent epidemiologic research has been inconclusive regarding the associations of physical activity and obesity with pancreatic cancer. Of seven studies on physical activity and pancreatic cancer, four reported no association (11, 16-18) and three reported an inverse association (10, 19, 20). Since 2000, six studies of obesity and pancreatic cancer incidence reported no association (11, 16, 17, 19, 21, 22), whereas six others reported a positive association (7, 10, 20, 23-25).

There is a plausible biological pathway through which physical inactivity and obesity could lead to pancreatic cancer.

Table 1. Baseline characteristics of women who did or did not develop pancreatic cancer, 1986

	Incident pancreatic cancer		P
	Yes (n = 209)	No (n = 37,793)	
Mean age, y (SD)	62.4 (4.3)	61.6 (4.2)	0.01
Mean BMI, kg/m ² (SD)	27.1 (5.1)	27.0 (5.1)	0.86
Mean WHR (SD)	0.84 (0.08)	0.84 (0.09)	0.33
BMI categories			
Normal weight (BMI < 25 kg/m ²)	84 (40%)	14,962 (40%)	0.71
Overweight (25-29.9 kg/m ²)	72 (34%)	13,956 (37%)	
Obese (≥ 30 kg/m ²)	53 (25%)	8,875 (23%)	
WHR tertiles			
≤ 0.7951	69 (33%)	12,533 (33%)	0.30
0.7952-0.8693	61 (29%)	12,571 (33%)	
≥ 0.8694	79 (38%)	12,520 (33%)	
Regular physical activity			
Yes	121 (58%)	21,767 (58%)	0.87
No	88 (42%)	15,468 (42%)	
Physical activity level			
Low	97 (46%)	17,534 (47%)	0.17
Medium	49 (23%)	10,222 (28%)	
High	63 (30%)	9,269 (25%)	
Moderate physical activity			
Few times a year, rarely or never	40 (19%)	7,694 (21%)	0.83
1 time a week or a few times a month	58 (28%)	10,558 (28%)	
≥ 2 times per week	111 (53%)	4,476 (12%)	
Vigorous physical activity			
Few times a year, rarely or never	176 (84%)	30,777 (83%)	0.79
1 time a week or a few times a month	18 (9%)	3,222 (9%)	
≥ 2 times per week	15 (7%)	3,157 (9%)	
Smoking status			
Current smoker	47 (23%)	5,504 (15%)	0.002
Former smoker	29 (14%)	7,178 (19%)	
Never smoker	129 (63%)	24,512 (66%)	
Pack-years of smoking			
0	129 (64%)	24,512 (66%)	0.38
1-19	24 (12%)	5,001 (14%)	
20-39	27 (13%)	4,143 (11%)	
>40	23 (11%)	3,215 (9%)	
Diabetes			
Yes	25 (12%)	2,338 (6%)	0.0006
No	183 (88%)	35,150 (94%)	
Alcohol (g/d)			
0	113 (54%)	21,353 (57%)	0.78
≤ 4	52 (25%)	8,886 (24%)	
>4	44 (21%)	7,554 (20%)	
Coffee			
Never or rarely	127 (61%)	21,510 (58%)	0.32
Once or more per month	28 (14%)	4,155 (11%)	
Once or more per week	27 (13%)	5,970 (16%)	
Once or more per day	25 (12%)	5,449 (15%)	
Tea			
Never or rarely	84 (43%)	14,858 (42%)	0.18
Once or more per month	23 (12%)	5,952 (17%)	
Once or more per week	47 (24%)	8,753 (24%)	
Once or more per day	42 (21%)	6,190 (17%)	
NSAIDs and aspirin use			
No	28 (22%)	5,185 (18%)	0.24
Yes	102 (78%)	24,281 (82%)	
Multivitamin use			
No	152 (74%)	24,700 (66%)	0.02
Yes	53 (26%)	12,483 (34%)	

Abbreviation: NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 2. HRs and 95% CIs for incident pancreatic cancer in relation to BMI, waist circumference, WHR, and physical activity

Characteristic	Cases	Person-years	Age-adjusted HR (95% CI)	Multivariate HR* (95% CI)
BMI (kg/m ²)				
<25.0	84	225,020	1.00 (reference)	1.00 (reference)
25.0-29.9	72	213,064	0.90 (0.65-1.23)	0.94 (0.69-1.29)
≥30.0	53	133,162	1.07 (0.76-1.51)	1.14 (0.81-1.62)
WHR				
0.335-0.7951	69	193,117	1.00 (reference)	1.00 (reference)
0.7952-0.8693	61	190,769	0.87 (0.61-1.22)	0.86 (0.61-1.21)
0.8694-2.8361	79	184,964	1.14 (0.82-1.58)	1.12 (0.81-1.55)
Regular physical activity				
No	121	326,583	1.00 (reference)	1.00 (reference)
Yes	88	236,296	0.98 (0.75-1.29)	1.08 (0.81-1.42)
Physical activity level				
Low	97	261,774	1.00 (reference)	1.00 (reference)
Medium	49	155,948	0.83 (0.59-1.17)	0.88 (0.62-1.24)
High	63	142,086	1.16 (0.85-1.60)	1.29 (0.93-1.77)
Moderate activity				
Few times a year, rarely or never	40	112,398	1.00 (reference)	1.00 (reference)
1 time a week or a few times a month	58	160,282	1.01 (0.68-1.51)	1.06 (0.71-1.58)
≥2 times per week	111	292,654	1.03 (0.72-1.48)	1.14 (0.79-1.65)
Vigorous activity				
Few times a year, rarely or never	176	464,188	1.00 (reference)	1.00 (reference)
1 time a week or a few times a month	18	49,562	0.98 (0.60-1.59)	1.02 (0.63-1.66)
≥2 times per week	15	48,016	0.85 (0.50-1.43)	0.93 (0.55-1.57)

*Adjusted for age (continuous), smoking status (current, former, and never), and multivitamin use.

Obesity and physical inactivity are well-established risk factors for insulin resistance and type II diabetes (8, 9). Insulin resistance has been shown to induce islet cell proliferation and turnover, which in turn promotes pancreatic carcinogenesis (3, 26).

The next step for research in this area may be to pool data across several cohort studies that have addressed this hypothesis to increase power. Nevertheless, in this cohort, there was no evidence that obesity or physical inactivity play a role in pancreatic cancer etiology.

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