Physical Activity and Proliferative Retinopathy in People Diagnosed With Diabetes Before Age 30 Yr

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OBJECTIVE — To examine the relationships of past and current physical activity to the prevalence of PDR.

RESEARCH DESIGN AND METHODS — Individuals diagnosed with diabetes <30 yr of age (n = 818), who were participants in the population-based Wisconsin Epidemiologic Study of Diabetic Retinopathy, were examined during 1984–1986. Stereoscopic fundus photographs were graded for presence of PDR. Physical activity was assessed by an interviewer-administered standardized questionnaire.

RESULTS — Women diagnosed with diabetes <14 yr of age who reported a history of participation in team sports in high school or college were less likely to have PDR at examination (OR 0.46, 95% CI 0.23,0.93). Those women who reported current strenuous activity levels were less likely to have PDR (OR 0.34, 95% CI 0.13,0.87). There were no significant associations between past or current physical activity and PDR in men. Current levels of energy expenditure were not related to PDR in either sex.

CONCLUSIONS — Higher levels of physical activity may be associated with a reduced risk of having PDR in women. However, the lack of similar findings in men suggests that physical activity may be a relatively unimportant factor in the etiology of PDR.

PDR is a common complication affecting people with diabetes. In the Wisconsin Epidemiologic Study of Diabetic Retinopathy, 67% of people diagnosed with diabetes when <30 yr of age had developed PDR after ≥35 yr duration of diabetes (1). Identification of modifiable life-style factors associated with PDR might lead to new interventions to prevent this vision-threatening disorder.

Leisure-time physical activity is associated with lower risks of mortality and cardiovascular disease morbidity in nondiabetic people (2–4) and in people with IDDM (5–8). However, there are few data describing the relationship of physical activity with the microvascular complications of diabetes. One questionnaire survey of a cohort identified from a hospital-based registry found no association between history of participation in team sports and history of laser treatment or blindness in males (6). Recently, this same group found no association between historical physical activity during the high school and college years and PDR (8). We are unaware of any other epidemiological studies addressing this issue.

As part of the large population-based Wisconsin Epidemiologic Study of Diabetic Retinopathy, we ascertained reported physical activity levels to determine whether past or current physical activity was associated with the prevalence of PDR.

RESEARCH DESIGN AND METHODS

— The population and methods have been described previously (1,9,10). Briefly, a population-based prevalence cohort of 10,135 people with diabetes was identified during 1979–1980 from an 11-county area in southern Wisconsin (Health Service Area 1). A sample of 2990 individuals, including all 1210 who had been diagnosed with diabetes <30 yr of age and were taking insulin, was asked to participate in the examination phase. During 1980–1982, 82.3% of these younger-onset patients participated in the baseline examination. Four years later, 891 of 996 (89.5%) younger-onset participants in the baseline examination were seen for follow-up examination, 64 (6.4%) had died, 12 (1.2%) had an interview only, 4 (0.4%) could not be located, and 25 (2.5%) re-

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OR, ODDS RATIO; CI, CONFIDENCE INTERVAL; PDR, PROLIFERATIVE DIABETIC RETINOPATHY; IDDM, INSULIN-DEPENDENT DIABETES MELLITUS.

Table 1—*Characteristics of study group at follow-up examination, 1984–1986*

	MEN		WOMEN	
	N	MEAN ± SD	*N*	MEAN ± SD
AGE (YR)	408	32.7 ± 1.13	410	33.4 ± 11.5
DURATION OF DIABETES (YR)	408	17.3 ± 8.8	410	18.9 ± 9.7*
AGE AT DIAGNOSIS (YR)	408	15.4 ± 7.4	410	14.5 ± 7.1
HbA_1 (%)	395	10.0 ± 1.9	389	10.1 ± 1.9
BODY MASS INDEX (KG/M^2)	382	24.8 ± 3.4	395	25.0 ± 4.3
PDR (%)		31.4 (128)		26.7 (109)
PARTICIPATION IN TEAM SPORTS REPORTED (%)		65.7 (268)		43.7 (179)†

Values in parentheses are *n*.
*$P < 0.05$.
†$P < 0.001$.

fused. All analyses were confined to data collected at the time of follow-up examination (1984–1986).

Participants underwent an examination, which included measurements of height, weight, blood pressure with the Hypertension Detection and Follow-up Program protocol (11), and refraction and best-corrected visual acuity with the Early Treatment of Diabetic Retinopathy protocol modified for a distance of 2 m (12). GHb level was determined with a resin microcolumn technique (13). Stereoscopic color fundus photographs of seven standard fields were taken of each eye. These photographs were graded in a masked fashion for the presence and severity of retinopathy with a modification of the Airlie House Classification scheme (14,15).

For this study, individuals were classified as PDR if they were rated as level ≥60 in at least one eye. This level consists of fibrous proliferations, new vessels, vitreous or preretinal hemorrhage, or scars of photocoagulation either in scatter or confluent patches, presumably directed at new vessels.

For each eye, visual acuity was recorded as the number of letters read correctly from 0 (<20/200) to 70 (20/10). For analyses, participants were grouped into those without visual impairment based on visual acuity in the better eye (better than 20/40; ≥41 letters correct) and those with visual impairment (20/40 or worse; 40 or fewer letters correct).

A medical history interview was conducted by trained examiners ($n = 6$) during which people ($n = 818$) who had completed at least a ninth-grade education were asked: "Do (did) you participate in team sports in high school or college?" The 73 subjects with less than a ninth grade education were not asked this question. Estimates of current activity patterns were also obtained. Participants were asked whether they participated, at least once a week, in a regular activity such as brisk walking, jogging, or bicycling long enough to work up a sweat; whether they participated in sports or recreation in the past week or in the past year; how many blocks they walked each day; how many flights of stairs they climbed each day; and to rate their activity at home, work, or school as sedentary, moderate, or strenuous. Participants with leg amputations ($n = 14$) were excluded from analyses of current activity.

The Harvard Alumni Activity Survey (2) was administered to a random sample of the cohort ($n = 404$), who were selected for a genetic marker study (16). This questionnaire ascertains leisure time sports activities (type, frequency, and amount of time spent in each activity) in the past week and the past year to allow for seasonal variation. Kilocalories of energy expenditure per week from light, medium, and hard sports activities were combined with the energy expenditure from flights of stairs climbed and blocks walked to arrive at a measure of average energy expenditure in kilocalories per week. This measure of physical activity was transformed with the square root before statistical analysis.

For this study, participants were considered to have other complications if they had proteinuria at exam (urine protein concn ≥30 mg/dl by Labstix) or reported a history of myocardial infarction, stroke, angina, renal transplant, renal dialysis, toe amputation(s), numbness, tingling, or loss of sensation in hands or feet; decreased temperature sensitivity; leg-hair loss; or sores or ulcers on feet or ankles.

We used χ^2 statistics and the Mantel-Haenszel test of trend (17) to test the significance of differences in the distribution of PDR by physical activity measures. Student's *t* tests were computed to compare continuous variables between people with and without a positive history of participation in team sports. Logistic regression models were used to examine the odds of having PDR associated with a level of physical activity. All analyses were conducted with SAS (18,19).

RESULTS— The characteristics of the study group at the follow-up examination in 1984–86 are presented in Table 1. The duration of diabetes was slightly longer in women than in men. Women were less likely to report participating in team sports than men ($P < 0.001$).

PDR and historical physical activity

Given the young age of the study subjects, some were reporting history of past participation in team sports, whereas others may have been reporting current participation. To evaluate the association of past physical activity with PDR, subjects <23 yr of age or who reported still

Table 2—*Prevalence of proliferative retinopathy by history of participation in team sports in high school or college, age at diagnosis, and sex*

	Age at diagnosis (yr)											
	<14				14–29				Total			
	Males (N = 124)		Females (N = 154)		Males (N = 197)		Females (N = 183)		Males (N = 321)		Females (N = 337)	
	%	N	%	N	%	N	%	N	%	N	%	N
Participated in team sports												
Yes	57.5	42	30.8	20	27.5	38	22.9	19	37.9	80	26.4	39
No	49.0	25	48.3	43	25.4	15	21.0	21	36.4	40	33.9	64
	$P = 0.35$		$P = 0.029$		$P = 0.76$		$P = 0.76$		$P = 0.79$		$P = 0.14$	

being in school were excluded from these analyses of history of participation in team sports ($n = 160$).

Table 2 shows the prevalence of PDR by history of participation in team sports by sex. There were no significant associations overall for either men or women. However, some subjects were diagnosed with diabetes before high school, whereas others were diagnosed during or after these school years. Therefore, we stratified on age at diagnosis to examine the association of history of team sports with PDR in both groups.

Women diagnosed with diabetes before high school (age at diagnosis <14 yr of age) who later participated in team sports in high school or college were less likely to have PDR at the time of the examination ($P < 0.029$) (Table 2). There were no significant associations in men or women diagnosed after 14 yr of age.

In a logistic regression model with age and duration of diabetes as covariates, women diagnosed when <14 yr of age who then participated in team sports in high school or college were less likely to have PDR at follow-up than those who did not play team sports (OR 0.46, 95% CI 0.23,0.93). There were no significant associations between team sports and PDR in men or women diagnosed between 14 and 29 yr of age.

PDR and current activity

The relationships of current physical activity measures and PDR were examined in younger-onset participants ($n = 804$). People with amputations were excluded from analyses ($n = 14$). Table 3 presents the prevalence of PDR by current activity and sex. Women who considered themselves to have moderate or strenuous activity levels were less likely to have PDR than sedentary individuals ($P = 0.002$). The pattern was similar for men, although not statistically significant ($P = 0.07$). For both men and women, people who reported participation in regular activity long enough to work up a sweat, sports in the past week, or sports in the past year were less likely to have PDR than those not participating in these activities. The prevalence of PDR also was lower among those climbing more flights of stairs per day. In women, the prevalence of PDR was lower among those walking more blocks per day.

For a subset of subjects, estimates of current energy expenditure, as measured by the Harvard Alumni Activity Survey (2), were available. In both men and women, there was a lower prevalence of PDR in subjects with higher quintiles of energy expenditure ($P < 0.001$ for men and $P = 0.06$ for women).

After adjusting for the effects of age, duration of diabetes, and the presence of other complications in logistic regression models (Table 4), we found that women who rated their activity as strenuous were less likely to have PDR than sedentary women (OR 0.34, $P = 0.02$). There were no statistically significant associations between current physical activity and PDR in men. Current energy expenditure, as measured by the Harvard Alumni Activity Survey (2), was no longer associated with the prevalence of PDR after adjusting for the confounding effects of age and duration and presence of other diabetes complications.

In this study, 28.6% ($n = 30$) of women with PDR had visual impairment compared with 2.6% ($n = 8$) of people without PDR ($P < 0.001$). To control for the potential confounding effects of visual impairment, we restricted the analysis to those with normal vision. Self-rated level of physical activity continued to be associated with the prevalence of PDR in women (OR 0.33, 95% CI 0.11, 0.95; strenuous vs. sedentary, $P = 0.04$).

CONCLUSIONS— In this population-based study, women who were diagnosed with diabetes <14 yr of age and subsequently participated in team sports in high school or college, were less likely to have PDR at the time of the Wisconsin Epidemiologic Study of Diabetic Reti-

Table 3—*Prevalence of PDR by current activity measures and sex*

	Men (N = 398)			Women (N = 406)		
	PDR (%)	N	P	PDR (%)	N	P
Activity at home, work, or school						
Sedentary	38.9	35		38.6	39	
Moderate	27.6	63		22.6	60	
Strenuous	26.3	21	0.07*	15.8	6	0.001*
Sweat activity†						
Yes	25.2	64		20.5	48	
No	38.2	55	0.006	33.3	57	0.004
Sports in past week						
Yes	23.0	40		20.1	32	
No	35.3	79	0.008	29.7	73	0.03
Sports in past year						
Yes	25.5	83		21.9	62	
No	49.3	36	<0.001	35.3	43	0.005
Blocks walked/day						
0–1	49.1	28		38.8	38	
2–5	24.7	20		23.9	26	
6–11	17.8	13		18.3	11	
12–17	29.2	19		23.9	16	
≥18	31.9	37	0.30*	17.5	11	0.004*
Flights of stairs/day						
0–1	41.7	40		32.4	36	
2–4	29.0	29		30.1	37	
5–9	28.0	26		18.2	16	
≥10	22.2	24	0.004*	19.5	16	0.01*
Kilocalories/wk‡						
Quintile						
1§	48.8	20		36.8	14	
2§	34.2	14		37.5	11	
3§	26.8	11		20.0	8	
4§	22.0	9		20.5	8	
5§	14.6	6	<0.001*	19.5	8	0.06*

*Test of trend.

†"At least once a week did you participate in regular activity akin to brisk walking, jogging, bicycling, etc., long enough to work up a sweat?"

‡These data were collected on subset of study population (see METHODS) and only available for 205 men and 198 women.

§Quintiles correspond to the following levels of energy expenditure: men (1 = <625, 2 = 625–1413, 3 = 1414–2124, 4 = 2125–3515, 5 = ≥3516 kcal/wk); women (1 = <279, 2 = 279–609, 3 = 610–1094, 4 = 1095–2060, 5 = ≥2061 kcal/wk).

nopathy examination. Among all women diagnosed with diabetes when <30 yr of age, those who considered themselves to have strenuous levels of physical activity at home, work, or school were less likely to have PDR compared with sedentary women. These two findings suggest that physical activity may be associated with a decreased risk of PDR in women.

Physical activity may reduce the risk of PDR through its effects on blood pressure (20) and high-density lipoprotein cholesterol (4,21), factors also associated with retinopathy (22,23). Alternatively, our findings may be the result of bias. Girls with diabetes who were in poorer control, had early complications, or less healthy life-styles may have been less likely to participate in team sports. Women who maintained more active life-styles at follow-up may be less likely to have retinopathy because of other unmeasured factors.

The failure to find a relationship in men between historical physical activity and PDR is consistent with previous studies (6–8,24). However, the reasons for the positive association in women in our study, but not in Pittsburgh, is not clear. It is possible that this difference may be attributable to the larger sample size or older age distribution of our population.

Although history of participation in team sports during school years is a crude marker of physical activity levels, in our study (data not shown) and another study from Pittsburgh (6), participants in team sports had higher levels of energy expenditure at follow-up, as measured by the Harvard Alumni Activity Survey (2), than nonparticipants. In the recent report by Kriska et al. (8) subjects who reported participating in team sports in school also reported higher levels of energy expenditure during those years as measured by a historical activity questionnaire. These data suggest that this simple question may differentiate children with higher levels of physical activity from sedentary children.

Although we found significant univariate associations in both sexes with most of the measures of current activity, these relationships were no longer significant after adjusting for the confounding effects of age, duration of diabetes, and the presence of other complications. These data suggest that decreased levels of physical activity in subjects with PDR may be due to physical limitations imposed by comorbid conditions associated with the presence of PDR.

Although we do not find consistent associations between measures of current physical activity and PDR, participation in sports, activities leading to sweating, and the Harvard Alumni Survey focus primarily on leisure activities and may not accurately reflect total en-

Table 4—*Adjusted OR for relationships of current activity measures and PDR by sex*

	Men		Women	
	OR	95% Confidence interval	OR	95% Confidence interval
Activity at home, work, or school (strenuous vs. sedentary)	0.86	0.37,1.98	0.34†	0.13,0.87
Sweat (yes/no)	0.72	0.41,1.24	0.62	0.37,1.07
Sports in past week (yes/no)	0.71	0.41,1.22	0.71	0.41,1.21
Sports in past year (yes/no)	0.68	0.34,1.36	0.80	0.46,1.38
Blocks walked/day (12 blocks)	1.06	0.92,1.22	0.83	0.62,1.12
Flights of stairs climbed/day (10 flights)	0.79	0.53,1.19	1.01	0.87,1.36
Kilocalories/wk (1000 kcal)	0.65	0.36,1.18	0.91	0.44,1.89

*Adjusted for age, duration, and other complications.
†$P < 0.05$.

ergy expenditure. Work-related activity may be an important contributor to total energy expenditure in some populations (25). Our self-rated scale of physical activity at home, work, or school may be a better indicator of total energy expenditure than these measures of leisure activity.

Our failure to find significant relationships between physical activity and PDR in men may suggest that there are sex differences in the effects of physical activity in subjects with diabetes, perhaps due to hormonal influences. Alternatively, our measures of activity may be better at differentiating the very active from the sedentary in women than in men.

The lack of consistency across sex suggests that physical activity may be a relatively unimportant factor in determining who develops PDR. However, it is important to note that this large study found no evidence that physical activity may be detrimental to people with diabetes. Our study and those from Pittsburgh (6–8,24) found no adverse associations between physical activity and PDR. Instead, there is evidence that physical activity may be associated with a reduced risk of many of the complications of diabetes. Longitudinal studies with activity measures are needed to address the temporal relationships between physical activity and diabetic complications and to further examine sex differences in these associations.

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