LITERATURE REVIEW

Physical Activity, Obesity, Height, and the Risk of Pancreatic Cancer

John Kirkpatrick MA, MD


Address: Aid Association for Lutherans, 4321 North Ballard Road, Appleton, WI 54919-0001.

Correspondent: John E. Kirkpatrick, MD, 2nd Vice President and Associate Medical Director.

Key words: Pancreatic cancer, risk factors, obesity, height, physical activity.

Pancreatic cancer is the 5th leading cause of cancer-related mortality in the United States. Smoking has been the strongest environmental factor linked to pancreatic cancer. Many studies have shown an association between diabetes mellitus and pancreatic cancer. More recently, a positive association between impaired glucose tolerance and pancreatic cancer risk was identified. This may be suggesting that impaired glucose tolerance, insulin resistance, and hyperinsulinemia play a role in the etiology of pancreatic cancer. This study examines the risk of pancreatic cancer to obesity, increased height, and physical activity.

STUDY DESIGN

Two large prospective cohort studies were used in this study. The Health Professionals Follow-up Study (NHFS) and the Nurses Health Study (NHS) were used for analysis. The HPFS was begun in 1986 with 51,529 men enrolled. The NHS began in 1976, with more than 120,000 female RNs having been mailed questionnaires. Information was gathered at baseline and every 2 years in follow-up. Deaths were reported by family members and the National Death Index.

Baseline weight, current weight, weight at age 21, and weight change within the past 5 years were gathered by self-reported data. A small number of patients were measured by technicians, who found a .97 correlation for men and .96 correlation for women in self-reported weight data.

Physical activity was assessed by asking participants to quantify time spent in each of 8 areas: walking, jogging, running, bicycling, swimming, tennis, calisthenics, and aerobic dance. The evaluation did not include household or occupational physical activities.

RESULTS

In a total of 2,800,837 person-years of follow-up from the 2 cohorts, there were 140 male and 210 females diagnosed with pan-
creatic cancer. There was a statistically significant association between BMI and the risk of pancreatic cancer. After adjusting for smoking and diabetes, those with a BMI >30 had a 72% increase in the incidence of pancreatic cancer compared with men and women with a BMI <23. An increase of 1 BMI was associated with a 3% increase in pancreatic cancer in the NHS and a 5% increase in the NPFS.

Height

There was an association between height and pancreatic cancer in both cohorts. Combining men and women, the highest category of height had a Relative Risk (RR) of 1.81 compared with the lowest category of height. This remained statistically significant even after adjusting for known risk factors and BMI.

Physical Activity

There was an inverse association between physical activity and pancreatic cancer. Vigorous activity did not alter the risk. Moderate activity was associated with a decreased risk of pancreatic cancer in both cohorts. Walking or biking more than 4 h/wk decreased the risk of pancreatic cancer by 54% compared with <20 min/wk. In the subset of BMI <25, physical activity had no noted effect on the incidence of pancreatic cancer.

SUMMARY

This study was a prospective design and consisted of a large sample size. The 2 cohorts were completely separate, yet the findings were similar. The observations confirmed an association between the risk of pancreatic cancer among obese men and women. Walking or similar activity was moderately associated with a 50% reduction in the pancreatic cancer risk. The role of obesity, insulin resistance, and hyperinsulinemia in the pathogenesis of pancreatic cancer is certainly a key issue. Improvements in these abnormalities continue to show benefit in many aspects of health, including the risk of pancreatic cancer.

In 1994, Dr Silverman reported that 25% of all pancreatic cancers were attributable to smoking. Michaud estimates an additional 15% may be due to obesity and inactivity. The question of whether a significant number of pancreatic cancers may be preventable with modest changes in weight, activity, and discontinuance of smoking is intriguing.
LITERATURE REVIEW

Albuminuria and Risk of Cardiovascular Events, Death, and Heart Failure in Diabetic and Nondiabetic Individuals

Michael Moore, MD, FACP


Address: Nationwide Insurance, One Nationwide Plaza, Columbus, OH 43215.

Correspondent: Michael Moore, MD, FACP, Vice President—Chief Medical Director.

Key words: Albuminuria, microalbuminuria, death, congestive heart failure, cardiovascular disease.

The presence of microalbumin has long been accepted as an early marker for the subsequent development of renal failure in diabetics. This study, as part of the Heart Outcomes Prevention Evaluation (HOPE) study, seeks to determine if there is a relationship between baseline microalbuminuria and the later development of cardiovascular (CV) disease in both diabetics and nondiabetics.

METHODS

Individuals enrolled were age 55 or older with a history of diabetes or cardiovascular disease. A total of 9043 individuals were enrolled, 3498 with diabetes, the remainder without. As part of the HOPE study, baseline measurements were obtained that included determination of microalbuminuria. Patients were then followed for 4.5 years. Measured endpoints were cardiovascular events (myocardial infarction, stroke, or cardiovascular death), death from any cause, and hospitalization for congestive heart failure (CHF).

RESULTS

The results showed a clear increase in cardiovascular events, all causes of death, and congestive heart failure in those patients who had microalbuminuria at the start of the study. In the Table is illustrated the rise in these endpoints for all participants as well as fractionated into the diabetic and nondiabetic subgroups.

DISCUSSION

As can be seen from the chart, there is a clear-cut increase in cardiovascular events, death, or development of congestive heart failure when microalbumin was detected at the start of the study. It is important to remember, however, that none of the participants in the
Rise in Cardiovascular Events and Death

<table>
<thead>
<tr>
<th>Variables</th>
<th>With Microalbuminuria (%)</th>
<th>Without Microalbuminuria (%)</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, stroke, or cardiovascular death</td>
<td>23.1</td>
<td>13.8</td>
<td>1.83</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>18.2</td>
<td>9.4</td>
<td>2.09</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>6.9</td>
<td>2.2</td>
<td>3.23</td>
</tr>
<tr>
<td>Diabetics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, stroke, or cardiovascular death</td>
<td>25.0</td>
<td>13.9</td>
<td>1.97</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>18.6</td>
<td>9.3</td>
<td>2.15</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>8.5</td>
<td>2.5</td>
<td>3.34</td>
</tr>
<tr>
<td>Nondiabetics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, stroke, or cardiovascular death</td>
<td>20.4</td>
<td>13.8</td>
<td>1.61</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>17.4</td>
<td>9.4</td>
<td>2.00</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>4.6</td>
<td>2.1</td>
<td>2.20</td>
</tr>
</tbody>
</table>

study would have been considered in excellent health at the start of the study because enrollment qualification included either the history of cardiovascular disease or diabetes. So while it is clear that, in this study, those individuals with initial baseline microalbuminuria did fare worse, one cannot draw conclusions from this study alone regarding the outcomes one might expect with respect to normal healthy individuals.
Relationship of Blood Pressure to 25-Year Mortality Due to Coronary Heart Disease, Cardiovascular Diseases, and All Causes in Young Adult Men

Kristi Petersen, MD


Address: American United Life Insurance, One American Square, Indianapolis, IN 46206.

Correspondent: Kristi Petersen, MD, Vice President and Assistant Medical Director.

Key words: Blood pressure, coronary artery heart disease, mortality.

The risk relationship of blood pressure (BP) to major cardiovascular diseases (CVD) has been well studied in middle aged and older populations. As risk factors, both systolic and diastolic blood pressures (SBP, DBP) show a continuous and graded relationship that is predictive and consistent to coronary heart disease (CHD) and stroke, independent of other risk factors. Long-term observational studies in young adults have been limited to analyses of life insurance actuarial data or nested case-control investigations of former college students.

The Chicago Heart Association Detection Projects in Industry (CHA) included 10,874 men aged 18 to 39 years at baseline (1967–73). This group was followed for an average of 25 years. The research goals were to answer the following: Does SBP, DBP, and SBP/DBP predict long-term mortality due to CHD, CVD and all causes for young men? Is SBP a better predictor than DBP? And what long-term risks, absolute excess risks, and impairment of life expectancy is there in young men with higher BP compared with those risks in young and middle aged men. Baseline data included age, sex, ethnicity, education, BP, total cholesterol, smoking status, height, and weight. A resting electrocardiogram was done and a medical history was taken. The exclusion criteria included missing data at baseline or on follow-up, baseline EKG evidence of myocardial infarction, history of myocardial infarction or other CHD, antihypertensive drug treatment at baseline or previously diagnosed diabetes mellitus. The cohort was divided into categories following the JNC-VI classification of BP:

- Optimal (SBP < 120, DBP < 80)
- Normal (SBP 120–129, DBP < 85 or SBP < 130, DBP 80–84)
- High normal (SBP 130–139, DBP < 90 or SBP < 140, DBP 85–89)
- Stage 1 HTN (SBP 140–159, DBP < 100 or SBP < 160, DBP 90–99)
Stage 2 HTN (SBP 160–179, DBP < 110 or SBP < 180, DBP 100–109)
• Stage 3 HTN (SBP ≥ 180, DBP ≥ 110).

The reference group for this study included those with normal (not optimal) BP. The relationship was calculated between baseline BP and the age-adjusted 25-year mortality from CHD, CVD, and all-cause mortality. Multivariate-adjusted hazard ratios (HRs) were calculated using the Cox proportional hazard regression. The HRs were adjusted for age, race, education, serum total cholesterol, smoking status, body mass index (BMI), and any EKG abnormality. At baseline, 8.6% of the cohort had optimal BP, 20.2% had normal BP, 25.5% had high normal, and 36.4% had stage 1 hypertension.

RESULTS

The age-adjusted death rates and multivariate-adjusted HRs were lowest for those with normal, but not optimal, blood pressures. There was a progressive increase in the adjusted rates and HRs for the defined strata above normal BP. The HRs for CHD were 1.37 for the high-normal stratum and 1.62, 2.51, and 3.60 for stages 1, 2, and 3 hypertension, respectively, as compared with the normal stratum. For those with optimal BP at the outset, 45 of 59 deaths in this stratum were due to noncardiovascular causes, with about half of these deaths being due to neoplasm. Overall, the high-normal and stage 1 hypertension strata accounted for 58.7% of excess CVD deaths and 59.4% of excess deaths due to all causes.

DISCUSSION

This article references Society of Actuaries (SOA) studies of BP levels and mortality risks for 4 million entrants ages 15–69 years published in 1959 and 1980. The SOA studies showed a similar continuous and graded relationship of SBP/DBP to mortality in entrants aged 20–29 and 30–39. It was noted that the SOA data were not multivariate adjusted and “may have had limitations related to accuracy of BP measurements in insurance examinations.” This reviewed study of young adults from the general (working) population shows a significant independent association of BP level and CHD and CVD mortality. The authors noted a limitation of their study was that the results were based on a single BP measurement, and because of this limitation, the associations could be underestimated. I would comment that, because diabetics, hypertensives under treatment, and anyone with EKG evidence of a prior MI were excluded from the study, the relationship of BP to CVD and CHD mortality could be dramatically understated. The mortality risk is shown to be graded and significant even for those without obvious comorbidities. There are those that indicate our industry can forego APSs and medical exams for applicants less than 40 years old. There are economic pressures to decrease expenses. Yet large prospective studies, both in our industry and in the clinical literature, have shown things as simple as a single BP measurement can help us stratify risk.