Cigar consumption has been increasing in the United States since 1993. There are several likely reasons for this increase, including promotion by the mass media and the belief that cigar smoking is generally thought to be safer than cigarette smoking. The association of cigar smoking with cancer of the oropharynx and the upper aerodigestive tract and chronic obstructive pulmonary disease (COPD) has been well documented by a number of studies. However, the association of cigar smoking with cardiovascular heart disease (CHD) has not been determined definitively.

This article reported a retrospective study that evaluated the association of cigar smoking with several disorders. Although the study has some limitations that are common with retrospective studies, it is well thought out and well designed. It offers substantial evidence that cigar smoking is associated with an increased risk of COPD and related conditions and CHD and that cigar smoking is associated with an increased risk of cancer of the oropharynx and lung cancer. It also offers support for an apparent dose-response (number of cigars smoked daily) association with multiple disorders.

The study cohort was a subpopulation of 17,774 men aged 30 to 85 years enrolled in the Kaiser Permanente Medical Care Program of Northern California. They were selected from a larger population of 207,165 members (46% male, 54% female) aged 14 and up that had had voluntary health examinations at the time of their enrollment from 1964 through
Table 1. Incidence and Risk of Cardiovascular Heart Disease and Chronic Obstructive Pulmonary Disease in Relation to Cigar Smoking

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative Risk for Cigar Smokers vs Non-Cigar Smokers, Age-Adjusted (95% CI)*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease</td>
<td>1.27 (1.12–1.45)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>1.07 (0.85–1.34)</td>
<td>.55</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>1.12 (0.67–1.90)</td>
<td>.65</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>1.29 (0.84–1.98)</td>
<td>.23</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease and related conditions</td>
<td>1.45 (1.10–1.91)</td>
<td>.008</td>
</tr>
</tbody>
</table>

* CI indicates confidence interval.

1973. Entry was limited to men who reported never smoking cigarettes and were not pipe smokers at the time they entered the study. Women were not studied because of an inadequate number of entrants (only 25 reported smoking cigars and not cigarettes or a pipe). Of the 17,774 entrants, 8.7% (1546) currently smoked cigars; 91.3% (16,228) did not currently smoke cigars and were used for the control population.

Cigar smokers were stratified by daily consumption: <5 cigars daily, 5–10 cigars daily, and >10 cigars daily. No information was available about the length of time cigars had been smoked, the degree of inhalation, or the type of cigar usually smoked. No history of cigar or pipe smoking was asked, so former cigar and pipe smokers would have been in both groups (cigar smokers and the control population).

If more than one health check-up was available, the first one was used. Several baseline measurements were taken: (1) serum cholesterol; (2) self-reported alcohol use stratified by daily consumption: none, 1–2 drinks daily, 3–5 drinks daily, and 6 or more drinks daily; and (3) presence or absence of diabetes mellitus, cardiovascular disease, or COPD based on patient history.

Follow-up for the development of cancer was done using hospitalization records and tumor registries. COPD and CHD follow-up was done using hospital discharge files. Habits followed up included the continuation of cigar smoking and switching to or the addition of cigarette smoking. Age-adjusted rates were used in the statistical analyses. Multivariate analysis of cancer and COPD included the following covariates: age, race, body mass index, history of diabetes mellitus, current alcohol consumption (stratified), and any recent or past occupational exposure (to airborne pollutants). The multivariate analysis of cardiovascular disease also included the following covariates: education (no college vs any college), systolic blood pressure, and total serum cholesterol.

RESULTS

Person-years of follow-up were 228,512 for non-cigar smokers and 20,176 for cigar smokers. Cigar smokers were more likely to have no college education and had significantly higher alcohol consumption. By history, of 17,774 entrants, 485 had CHD only, 657 had COPD only, 53 had CHD and COPD and 16,579 reported neither CVD nor COPD. Of 1546 cigar smokers, 76% (1177) smoked <5 cigars daily, 17% (263) smoked 5 or more daily, and for 7% (106), the number smoked daily was unknown.

The relative risk using age-adjusted rate of occurrence per 10,000 person years was higher for cigar smokers (relative to the control group) for COPD and related conditions and for CHD (Table 1). There was no association with ischemic or hemorrhagic stroke or peripheral artery disease.

Cigar smokers had an increased risk for
Table 2. Incidence and Risk of Cancer in Relation to Cigar Smoking

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative Risk for Cigar Smokers vs Non-Cigar Smokers, Age-Adjusted (95% CI)*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer of the oropharynx</td>
<td>2.61 (1.18–5.76)</td>
<td>.02</td>
</tr>
<tr>
<td>Cancer of the upper aerodigestive tract</td>
<td>2.02 (1.01–4.06)</td>
<td>.04</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>2.14 (1.12–4.11)</td>
<td>.02</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>1.21 (0.51–2.88)</td>
<td>.66</td>
</tr>
<tr>
<td>Cancer of the kidney</td>
<td>1.08 (0.43–2.71)</td>
<td>.87</td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>1.05 (0.55–2.01)</td>
<td>.89</td>
</tr>
<tr>
<td>All smoking-related cancers</td>
<td>1.42 (1.02–1.98)</td>
<td>.04</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>1.12 (0.80–1.57)</td>
<td>.51</td>
</tr>
<tr>
<td>All cancer (except nonmelanoma skin cancer)</td>
<td>1.07 (0.93–1.25)</td>
<td>.35</td>
</tr>
</tbody>
</table>

* CI indicates confidence interval.

cancer of the oropharynx, upper aerodigestive tract, or lung (Table 2). The relative risk for all smoking-related cancers was only marginally significant (note that the lower 95% confidence interval is only 1.02). There was no significant difference of the other cancers studied or all cancers combined.

Cigar smokers were stratified into <5 cigars daily and ≥5 cigars daily to determine if there is a dose-response relationship (Table 3). For the ≥5 cigars group, the risk of CHD, COPD, and cancer of the lung and upper aerodigestive tract was statistically significant, whereas it was not (statistically significant) for those that smoke <5 cigars daily. The same was observed for all smoking-related cancers but not for all cancers combined. There was a marginally increased risk of peripheral arterial disease for patients who smoked 5 or more cigars daily.

As compared to studies of cigarette smoking, the relative risks for COPD and lung cancer were less for cigar smokers. However, the authors pointed out a confounding factor that underestimates the risk of cigar smoking in this study. Smoking habits for the cohort are determined at the beginning of the study with incomplete follow-up. At 4-year and 8-year rechecks, where 28% (438) and 11% (171) of the cigar-smoking cohort reported, respec-
tively, 64% (281) and 50% (86), respectively, reported that they still smoked cigars. Incomplete follow-up would tend to overestimate the exposure (since not every cigar smoker persisted in smoking cigars) and as a result, underestimate the risk.

Additionally, in this study, cigar smokers have significantly higher alcohol consumption than the control population. The higher alcohol use in cigar smokers is a confounding factor because alcohol has been associated with an increased risk for oropharyngeal cancer and the upper aerodigestive tract in cigarette smokers.
LITERATURE REVIEW

Palindromic Rheumatism and the Risk for Rheumatoid Arthritis

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Key Words: Rheumatoid arthritis, rheumatoid factor, palindromic rheumatism, prognosis.

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Palindromic rheumatism can evolve into rheumatoid arthritis (RA) or connective tissue disease (CTD). It is defined as the presence of episodic attacks of joint pain accompanied by signs of joint inflammation with complete remission between episodes. It can affect a single joint or many joints; it may last hours to days; and it may recur with a frequency of weeks to months.

This study was based upon a cohort with the diagnosis of palindromic rheumatism referred to rheumatologists at the University of Alberta. This cohort was studied between 1986 and 1996.

STUDY METHODOLOGY

This was a retrospective study of a population of 127 people who met documented inclusion criteria for the diagnosis of palindromic rheumatism. They were identified from over 4900 referrals to the University of Alberta for arthritis. The criteria included normal radiographs and the exclusion of other recurrent monoarthritis such as gout and chondrocalcinosis. This cohort was studied between 1986 and 1996.

Variables of interest included the number and identity of joints involved, frequency of attacks, duration of attacks, and presence of rheumatoid factor. The duration of palindromic rheumatism was estimated from the time of initial attack until the development of RA or CTD or until the last consultation if the patient did not evolve another systemic rheumatologic disease.

Differences in this “survival time” (free of RA or CTD other than palindromic rheumatism) were evaluated using Kaplan-Meier methods. Cox proportional hazard models were used to identify variables associated with the development of RA or other CTD. Both univariate and multivariate Cox regression analyses were performed.

RESULTS

Women comprised 65% of the 127 subjects. The mean age at onset of attacks was 40
years. The mean duration of symptoms was 6 years. The most commonly involved joints were: wrist (65% of patients), knee (60%), metacarpophalangeal (56%), and shoulder (35%). The rheumatoid factor (RF) was positive in 39% of patients. Forty-three (34%) of the study group developed rheumatoid arthritis or a connective tissue disease during the period of observation.

A comparison of the clinical findings found in those who developed RA or CTD with those who did not revealed no significant difference in mean age at onset (ages 42 and 38, respectively), sex, number of attacks (18 and 13), length of attacks (4 days), or frequency of knee involvement. There was a statistically significant association between involvement of the wrist, proximal interphalangeal joints (PIP), and metacarpophalangeal (MCP) joints, with subsequent development of RA or CTD. A positive rheumatoid factor had the most significant association with development of rheumatoid arthritis (no RA/CTD 29% positive RF; RA/CTD 57% positive RF; \( P = .003 \)).

The hazard ratio of developing RA or CTD was 2.9 in patients with positive RF compared with negative patients. For women with hand or wrist arthritis and a positive RF, the hazard ratio was 8.0 compared with patients with 1 fewer of these 3 features.

The survival time without development of RA or CTD showed significant differences for the top quartile (75% without RA or CTD) for the clinical features of a positive RF and for involvement of hand joints. RF-positive patients had a survival time of 32 months vs 91 months for RF-negative patients. Similarly, the top quartile with involvement of the MCPs survived 35 months vs 82 months without MCP arthritis.

**DISCUSSION**

Rheumatoid arthritis has multiple patterns of onset. This spectrum ranges between a gradual onset, with small joint stiffness increasing over months, to an abrupt polyarthritis with intense pain and incapacitation. Palindromic rheumatism lies in between these presentations.

Palindromic rheumatism may have features of many of the American Rheumatism Association criteria (1987) for the diagnosis of rheumatoid arthritis. This diagnosis is made by satisfying 4 of 7 criteria, which include the clinical features of (1) polyarthritis of 3 or more joints, (2) morning stiffness of 1 hour or more, (3) symmetric arthritis, and (4) wrist, MCP, or PIP involvement. In palindromic rheumatism, these features may be present but only briefly, far short of the 6-week duration required for meeting the criteria. The other diagnostic criteria for rheumatoid arthritis—(5) rheumatoid nodules, (6) a positive rheumatoid factor, and (7) radiographic changes of periarticular joint erosion or decalcification in the hand or wrist—need only be identified to meet one of the criterion.

In this study, 28% of those with palindromic rheumatism developed rheumatoid arthritis and 8% developed another connective tissue disease. Female sex alone was not predictive. Although involvement of the knee was commonly seen, it did not discriminate those who would evolve their palindromic rheumatism. On the other hand, 85% of those who developed RA or a CTD had wrist involvement and 71% had MCP involvement. Most predictive were the findings together of female sex, rheumatoid factor, and wrist involvement.

This study also documents the time course of palindromic rheumatism. Even in those with a positive rheumatoid factor and the worrisome history of episodic arthritis, it may take years to develop rheumatoid arthritis.

This retrospective study is limited by the likely referral bias inherent in university studies. Community patients with palindromic rheumatism may have less severe disease and be less likely to develop rheumatoid arthritis or another connective tissue disease than this study population. But as the largest cohort study of palindromic rheumatism, it identifies risk factors for the development of rheumatoid arthritis and other connective tissue disease and the course of onset.
Heart-Rate Recovery Immediately After Exercise as a Predictor of Mortality

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Exercise testing has long been a staple of the requirements for many life insurers for high-dollar life insurance policies. There has been considerable debate as to the usefulness of such testing given the rather limited specificity and sensitivity in those tests which are not supplemented with either thallium or echocardiography. Recently there have been several articles that have presented data that would seem to support the use of these simple, inexpensive tests as a predictor of mortality. This article is another example of such a study.

**BACKGROUND**

The expectation of exercise electrocardiography is that the heart rate will rise with increasing demands by increasing the elevation and speed of the treadmill. This increase is in part due to a reduction in tone from the vagus nerve. Slowing of the heart rate following cessation of exercise is due to vagal reactivation. Poor vagal activity is known to be a risk factor for mortality, and so the cardiologists at the Cleveland Clinic undertook a study to see if lack of slowing of heart rate following cardiac testing could be correlated with increased mortality.

**METHODOLOGY**

A total of 2428 adults (median age 57, 63% men) without a history of heart failure, coronary revascularization, or pacemaker were followed for a period of 6 years following diagnostic testing with SPECT exercise electrocardiography. A failure to reduce heart rate by at least 12 beats per minute at 1 minute into the recovery period was considered to be abnormal.
RESULTS

A total of 639 individuals met the above definition of abnormal in that they did not decrease their peak heart rate by at least 12 beats per minute after 1 minute of exercise cessation.

In 6 years of the study, there were 213 deaths from the 2428 total participants. Although only 26% (639) of the population tested had an abnormal result on testing, the majority of the deaths (56%) occurred within this group. This calculates to a relative risk of 4.0 for those having delayed heart rate recovery (confidence interval [CI] 3.0 to 5.2). Even after adjustments are made for age, sex, use of medications, abnormal thallium results, standard cardiac risk factors, resting heart rate, and workload achieved, the adjusted relative risk factor still remained twice that of those who had a normal heart rate recovery (adjusted RR = 2.0; CI 1.5 to 2.7).

DISCUSSION

The lack of vagus nerve recovery following exercise electrocardiography appears to be a strong predictor for mortality. When taken as the only factor, failure to reduce heart rate by at least 12 beats per minute 1 minute following exercise cessation is associated with a fourfold increase in risk of mortality. Even when other risk factors are considered such as the results of the SPECT exercise test, use of medicines or underlying disease, the relative risk is still twice baseline.

In conclusion, lack of vagus nerve reactivation designated by the failure to reduce the heart rate by at least 12 beats per minute after 1 minute of exercise cessation during stress electrocardiography is an independent predictor of mortality with a relative risk of 4.0 and an adjusted relative risk of 2.0.
Glucose Intolerance and 23-Year Risk of Coronary Heart Disease and Total Mortality

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It has been well established that there is an increased risk of total mortality and cardiovascular disease with type 2 diabetes. There is some controversy concerning the relationship between glucose intolerance and these outcomes.

This study by Rodriguez et al grew out of the Honolulu Heart Program, which has followed 8006 men of Japanese ancestry since 1965. The ages of these men ranged from 45 to 68 years at study entry. Coronary heart disease (CHD), stroke, and overall mortality was the study focus. The baseline examination of this cohort was done between 1965 and 1968 and included a medical and sociocultural history. Habits, dietary patterns, and physical activity were delineated. The dietary questionnaire looked at the extent the traditional Japanese diet was followed. The physical examination included body measurements. Laboratory values and other screening information included cholesterol, triglycerides, uric acid, glucose, routine urinalysis, hematocrit, FVC, FEV1, and a resting 12-lead electrocardiogram. A nonfasting 1-hour postload 50-gm glucose test was used to screen this population. It is noted that at this time, during the 1960s, these baseline laboratory studies and this glucose challenge were considered standard in epidemiologic studies. A postload “low-normal” glucose was defined as being <150 mg/dL, “high-normal” was 151–224 mg/dL, “asymptomatic high glucose” was considered to be >225 mg/dL, and the “known diabetes” category consisted of those who reported a history of diabetes regardless of glucose level and were being treated for diabetes or who had the diagnosis of diabetes and were not being treated but had a glucose level >225 mg/dL.
### Age- and Risk Factor-Adjusted RR of Total Mortality, Coronary Heart Disease (CHD) incidence, and CHD mortality by Glucose Tolerance Category*

<table>
<thead>
<tr>
<th>Variable</th>
<th>High Normal</th>
<th>Asymptomatic Hyperglycemia</th>
<th>Known Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.12 (1.02-1.23)</td>
<td>1.57 (1.36-1.81)</td>
<td>1.97 (1.70-2.30)</td>
</tr>
<tr>
<td>Risk factor-adjusted†</td>
<td>1.07 (0.97-1.18)</td>
<td>1.39 (1.20-1.61)</td>
<td>1.83 (1.56-2.14)</td>
</tr>
<tr>
<td>CHD incidence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.18 (1.01-1.38)</td>
<td>1.68 (1.33-2.12)</td>
<td>2.82 (2.27-3.50)</td>
</tr>
<tr>
<td>Risk factor-adjusted†</td>
<td>1.08 (0.92-1.27)</td>
<td>1.50 (1.18-1.90)</td>
<td>2.26 (1.80-2.84)</td>
</tr>
<tr>
<td>CHD incidence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.27 (0.98-1.63)</td>
<td>2.34 (1.70-3.24)</td>
<td>4.25 (3.16-5.72)</td>
</tr>
<tr>
<td>Risk factor-adjusted†</td>
<td>1.17 (0.91-1.50)</td>
<td>2.01 (1.44-2.81)</td>
<td>3.49 (2.56-4.75)</td>
</tr>
</tbody>
</table>

* Data are relative risk (95% confidence interval); low-normal group used as reference.
† Adjusted for age, pack-years of smoking, hypertension, alcohol intake, cholesterol, triglycerides, body mass index, and Japanese diet index.

All entrants were followed through a comprehensive hospital and death record surveillance system since entry into the study. Follow-up for mortality was virtually complete.

### RESULTS

During the 23 years of follow-up, the results revealed a stepwise increase in total mortality and CHD incidence and mortality with worsening glucose tolerance. The associations remained significant when the risk factors of age, smoking, alcohol intake, hypertension, total cholesterol, triglycerides, body mass index, and Japanese diet index were taken into account during the multivariable analysis. The study subjects that demonstrated low normal glucose levels were used as reference mortality. The results are seen in the Table.

### DISCUSSION

The results of this study confirm the relationship between postchallenge glucose intolerance and coronary heart disease and total mortality. The fact that this large population-based study did not use what we now consider the "gold standard" oral glucose tolerance test—ie, a fasting 2-hour glucose measurement after a 75-gm glucose load—is a potential limitation. It is possible that a stronger association between glucose tolerance, CHD, and total mortality would be observed if our current screening methods had been used. The screening technique also may have introduced enough variation to account for the failure to show an association between high normal glucose levels, CHD, and mortality, after the adjustment for risk factors was done.

In the insurance industry, we cannot always be assured that the client will be fasting when the blood is drawn for the required laboratory examination. If I may draw on clinical practice experience, few patients count coffee, soft drinks, or even toast or a bagel as breaking a fast. I would maintain that the screening technique used in this study is equivalent to our applicant population when they have a paramedical exam for insurance purposes. A 50-gm glucose load in a nonfasting study entrant is nearly the same as a nonfasting applicant who drinks 1 soft drink prior to a blood draw for an insurance laboratory. This study has more relevance to the insurance industry than initially might be thought: the glucose level is pertinent to risk assessment no matter what our clients consider to be fasting.
Cardiorespiratory Fitness and Mortality in Men

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The prevalence of obesity is increasing in the United States. This substantial increase had lead some to consider obesity as a modern epidemic. The correlation between obesity and mortality is certainly not a new one. This study attempts to address low cardiorespiratory fitness as an independent variable for cardiovascular disease deaths and all-cause mortality.

The data from this study are based on the Aerobics Center Longitudinal Study, a study associated with Kenneth Cooper and the Cooper Institute. They collected 25,714 patients over the period 1970–1993. The population was all male; 95% were white, and 80% were college graduates. Most were executives or professionals and considered to be in the mid- to upper socioeconomic strata.

The follow-up was “approximately 10 years,” although a minimum period of 1 year was required. The population was categorized by body mass index (BMI). Normal weight was considered to be a BMI of 18.5 to 24.9. Overweight was defined as a BMI of 25 to 29.9, and obesity was considered to be a BMI of >30.

The authors included 6 “mortality predictors” as study variables. Two of the mortality predictors were disease conditions; the presence of cardiovascular disease (CVD) and diabetes mellitus. The other 4 were increased serum cholesterol, hypertension, smoking, and low cardiovascular fitness. Cardiovascular fitness was determined by performance on a maximal exercise test on a treadmill. Subsets were defined by a MET cutoff point for low fitness: ages 20–39, 10.5 METS; ages 40–49, 9.9 METS; ages 50–59, 8.8 METS; and age >60, 7.5 METS.

There were 1025 deaths during the 258,781 man-years of follow-up. There were 439 deaths due to CVD, 43% of total deaths experienced. The baseline characteristics of the obese subset were that they had higher cholesterol, lower exercise tolerance, higher blood pressure, higher rate of physical inactivity, increased diabetes mellitus, and increased rate of CVD. The study calculated the relative risk
(RR) of CVD deaths and all-cause mortality as compared to the normal weight group. As compared with the normal weight group with no CVD, obese patients with a history of CVD have a RR of 14.0 for CVD death. The presence of any of the individual mortality predictors studied increased the age adjusted RR for CVD deaths by 4.4 to 5.0 (as compared with the normal weight group without that particular variable). There was a very strong trend of increased mortality as the BMI increased. All-cause mortality showed a similar trend. The presence of CVD was the strongest single variable in increasing the RR of all-cause mortality. The other 5 predictors showed an increase in RR from 2.7 to 3.1 in all-cause mortality (as compared with the normal-weight subset without that particular variable). In multivariate analysis, baseline CVD remained the most significant variable, as expected. The other 5 were similar in their influence on CVD death and all-cause mortality.

There are weaknesses to this study. The number of patients accumulated is impressive; however, the population was quite homogenous. Entrants were well-educated, white men in a high socioeconomic strata. The referral center is a unique facility well known for its emphasis on fitness. Whether or not these results can be reproduced in a more normal clinical setting should be pursued.

The conclusions of the study, given these limitations, are worthy of a trend impression. It is clear that as patients progress in BMI from normal to obese, there is a significant increase in both CVD deaths and all-cause mortality. The presence of CVD remains the most significant factor. Low cardiovascular fitness was as significant a factor as diabetes mellitus, increased cholesterol, hypertension and smoking.