Occasional Review

Coffee consumption and pancreatic cancer: temporal and spatial correlation

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Abstract

An examination of available data on per caput consumption of coffee and pancreatic cancer mortality in the United States since 1950 shows a temporal association. A rise and fall in coffee consumption was followed by a rise and fall in the incidence of pancreatic cancer with roughly a 10-year lag. Nevertheless, there were inconsistencies in this relationship by sex and race. An unimpressive spatial relationship was also found between the consumption of coffee and pancreatic cancer mortality in 13 countries. While this relationship suggests an association, major inconsistencies cast doubt on the possibility that it is one of cause and effect. This may be due to confounding, particularly by cigarette smoking. The association between cigarette smoking and cancer of the pancreas is much more consistent with a causal relationship.

Twenty-four thousand new cases of pancreatic cancer are expected in the United States in 1981. Currently this malignancy is the fourth most common cause of death from cancer in men and the fifth in women.¹ The importance of this neoplasm warrants intense investigation of its aetiology, especially since the cure rate currently remains negligible.

In 1977 we reported a cohort analysis of United States pancreatic cancer mortality for the 30-year period 1939-69.² We noted differences in the birth cohort cancer curves by race and sex. Successive birth cohorts showed increasing leftward shift of their age-specific mortality rate curves, indicating an increasing force of mortality for this disease that extended to younger cohorts until the turn of the century. This change was particularly pronounced in non-whites of both sexes, less prominent in white men, and practically non-existent in white women. Recent data up to 1978 have not changed these trends. We suggested that, in the search for environmental causes of pancreatic cancer, exposure characteristics should be compatible with these observations. Such causes might include smoking, occupational exposures, and diet.

Recently suspicion has settled on coffee as an aetiological factor of some significance. This was first suggested by Stocks in 1970 when he found a correlation between per caput consumption of coffee in 1965-6 and pancreatic cancer mortality in

1964-5 for 19 countries.³ This association was statistically highly significant in men but not in women.

In 1981 two case-control studies also suggested an association. Lin and Kessler⁴ reported a statistically significant association with the consumption of decaffeinated coffee among women but provided no specific data. MacMahon *et al*⁵ found a moderately strong association in both sexes.

If the association between pancreatic cancer and coffee is real then we would expect to be able to show both temporal and geographical correlations between these two variables, and the results should be consistent with our previous observations on cohort differences by sex and race. Accordingly we have examined available data on coffee consumption and pancreatic cancer mortality for temporal trends in the United States and for geographical correlation across countries, allowing whenever possible for lag periods to provide for cancer induction-latent periods.

Method

Data on coffee consumption in the United States were obtained from the National Coffee Association, New York. Since 1950 they have conducted telephone interview surveys of 7500 people aged over 10 in the 48 continental States 30 times. A two-stage probability design was used to select people for interview, as well as to designate a single, randomly selected respondent within each sample household. Daily consumption patterns have been calculated from these surveys.

For various countries around the world the National Coffee Association furnished us with data on the total number of bags of coffee imported, as well as the number of pounds per bag. Using a conversion factor of 55 cups per pound and population data for each country for the appropriate years, obtained from the United Nations Demographic Yearbook,⁶ we derived figures for cups/person/day. There is no breakdown by sex.

Data on pancreatic cancer mortality for 1978 were obtained from the Office of Health Research, Statistics, and Technology of the National Centre for Health Statistics for the study of United States temporal trends. Population data for 1978 were obtained from the Bureau of the Census, United States Department of Commerce.⁷ These data were used to calculate age-adjusted rates for the total population as well as by race and sex. The standard population for direct age-adjustment was the total 1950 United States population so that the rates could be compared with those of previous years from 1950 to 1973-4 published by Devesa and Silverman.⁸

Age-adjusted pancreatic cancer mortality over the period 1950-67 for various countries were obtained from the report by Segi and Kurihara.⁹

Results

TEMPORAL ASSOCIATION IN THE UNITED STATES

Figure 1 describes the trends in age-adjusted death rates for pancreatic cancer between 1950 and 1978 and coffee consumption between 1950 and 1980 in the United States. The incidence of cancer

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peaked in 1970 and has been declining since then. This decline in pancreatic cancer mortality does not support statements by others¹⁰⁻¹³ that the incidence of pancreatic cancer is increasing. Coffee consumption peaked in the early 1960s at about three cups/person/day and has since declined to about two cups/person/day. If the association is one of cause and effect these curves suggest that the induction-latent period may be about 10 years.

When the trend of the overall cancer death rate is examined by race and sex (fig 2), we find that white women have the lowest rates while non-white men have the highest. In non-white men the rates have levelled off in recent years while in white men there has been a definite decline. Although women of both races have shown a continuing increase in the rates non-white women have exhibited a four-fold greater increase than white women.

The trend in coffee consumption in the United States since 1958 (fig 3) by sex shows that differences between men and women in the average number of cups consumed per person per day are quite small

FIG 1—Trends of age-adjusted pancreatic cancer mortality from 1950 to 1978 and coffee consumption per caput from 1950 to 1980 in the United States.

FIG 2—Trends of age-adjusted pancreatic cancer mortality from 1950 to 1978 in the United States by race and sex.

FIG 3—Trends of coffee consumption per caput in the United States from 1958 to 1980 by sex.

and of little significance. The curves also show that both men and women have been consuming less since about 1962. Other data¹⁴ indicate that whites consume more than twice as much coffee as blacks. These observations are not consistent with the trends of pancreatic cancer by race and sex.

GEOGRAPHICAL ASSOCIATION

To ascertain whether there is any geographical relationship between coffee consumption and pancreatic cancer, we looked at both the incidence of and death rates for pancreatic cancer in those countries for which coffee consumption figures were available. Since cancer registry incidence rates¹⁵ are not available in many countries and those that are available vary in time to a fair degree, we have concentrated on age-adjusted death rates.⁹ Appropriate data for both coffee consumption per caput and pancreatic cancer death rates were available for 13 countries. The number in some comparisons was as low as 10.

The Pearson correlation coefficient (r) was used to describe the degree of relationship between the two variables (table), without and with lag periods to allow for a latent period between exposure and disease. Most of the coefficients lay between 0.50 and 0.68 but, because of small numbers, only two of these were statistically significant at the 0.05 level. The table presents the coefficients for men only. The values were almost the same in women, but this is to be expected because the correlation between male and female cancer incidence in the 13 countries was high ($r = 0.94$, $t = 8.79$, $p < 0.001$).

Correlation coefficients for male pancreatic cancer rates v coffee consumption by country with and without lag periods

Comparison periods		r	df	t	p
Pancreatic cancer	Coffee consumption				
1966-7	1966	0.52	11	2.01	NS
	1960	0.59	10	2.29	< 0.05
	1950	0.56	9	2.01	NS
1960-1	1960	0.39	10	1.35	NS
	1950	0.50	9	1.73	NS
1950-3	1950	0.68	8	2.63	< 0.05

Figure 4 illustrates a scattergram and regression analysis for the association in men, plotting pancreatic cancer mortality for 1966-7 against coffee consumption in 1960, one of the two comparisons that were statistically significant. The United States consumed the largest amount of coffee in the 1950s but by the 1960s the Nordic countries became the top consumers on a per caput basis, Finland and Sweden alternating as number one. Both Finland and Sweden had the highest mortality of cancer. At the lower end of the coffee consumption scale there is more variation in the mortality of pancreatic cancer. Despite relatively low coffee consumption, England and Wales, Israel, and Canada had a high mortality of cancer while both Italy and Japan had a low mortality. The correlation coefficient of 0.59 is not impressive.

FIG 4—Scattergram of male pancreatic cancer mortality in 1966-7 against coffee consumption per caput in 1960 for 12 countries.

Discussion

Several inconsistencies in the association between coffee and pancreatic cancer cast doubt on a cause-and-effect relationship. Our cohort analysis² showed a difference between white men and white women such that an increasing cohort effect in later birth cohorts was seen only in men. This would argue for a factor that differs in its impact on the sexes in whites. Such a factor is not likely to be an item like coffee, which is consumed equally by both sexes, unless one postulates a difference in susceptibility by sex.

The higher incidence of pancreatic cancer in non-whites is not consistent with what is known of their coffee consumption relative to that of whites. Therefore it would be difficult to attribute the pronounced increase in the incidence of pancreatic cancer among non-whites of both sexes to coffee unless one also postulates a difference in susceptibility by race.

In previous studies of the association between coffee and pancreatic cancer the results have been inconsistent. The spatial correlation found by Stocks³ was limited to men. The case-control study by Lin and Kessler⁴ found only an association between cancer and decaffeinated coffee, which was limited to women, whereas the case-control study by MacMahon *et al*⁵ found a fairly strong association in both sexes, no dose-response relationship in men and an irregular one in women.

Our current study also shows inconsistencies in the associations. Thus the temporal analysis of United States data suggests that after a lag period of about 10 years after the decrease in coffee consumption, the incidence of cancer in non-white men levelled and in white men declined. The incidence in women, however, has continued to rise. Once again, to keep the coffee-cancer hypothesis intact, you would have to postulate a difference in response to the agent by sex.

On the other hand, the spatial correlation by country in the current study is not impressive. Where it was possible to allow for a lag period, the coefficient was about the same with and without a lag. Although only two of six coefficients are statistically significant, small numbers are the primary reason. The probability of obtaining a *p* value of under 0.05 at least once by chance in six comparisons is 0.26.¹⁶

Consequently, in view of the inconsistencies detailed above, we must conclude that a cause-and-effect relationship between coffee and pancreatic cancer has not been established. Confounding of the association by another factor(s) must be seriously considered. Other agents associated with this neoplasm include cigarette smoking and occupational exposures.

In contrast to the coffee hypothesis, the evidence in favour of cigarette smoking as a significant aetiological factor is much more consistent and therefore more convincing. A review of the subject in the 1979 Surgeon General's *Report on Smoking and Health*¹⁷ analysed six prospective studies, all of which showed raised risks of pancreatic cancer in cigarette smokers relative to the risks in non-smokers. The relative risks ranged from 1.4 to 3.1. Two studies included data on women who also showed raised risk ratios of 1.9 and 2.5. Some of the studies, those with adequate numbers of cases, showed dose-response relationships. We can add the results of another prospective study, that of British physicians of both sexes.^{18, 19} These showed raised risks of pancreatic cancer among cigarette smokers, and the dose-response relationship in men was strong. In women the dose-response gradient was not completely consistent but the number of cases was quite small, 14 in all.

The temporal relationship between cigarette smoking and pancreatic cancer is quite consistent. In the United States men began to smoke cigarettes decades before women and the incidence in men began to decline after 1960, whereas the incidence in women declined only slightly in the late 1960s and then levelled off.²⁰ These temporal patterns are consistent with the trends in pancreatic cancer mortality by sex shown in fig 2.

Race and sex relationships for cigarette smoking in the United States are also consistent with the trends in pancreatic cancer mortality. Surveys of adults from 1965 to 1976²¹ showed that the

percentage of current regular cigarette smokers was higher in men than in women, higher in black men than in white men, and recently slightly higher in black women than in white women.

Probably, as Lin and Kessler pointed out,⁴ the aetiology of pancreatic cancer is multifactorial. There are some suggestions that occupational exposures may be of some importance.²²⁻²⁴ Occupational exposures may also confound to some degree the smoking-pancreatic cancer association, accounting for some of the race and sex differences.²⁵

We believe that prospective studies would be highly desirable to elucidate the relationship between coffee and pancreatic cancer, but very large populations and millions of dollars are required. Accordingly, additional case-control studies are warranted.

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References

- Silverberg E. Cancer statistics, 1981. *CA* 1981;**31**:13-28.
- Benarde MA, Weiss W. A cohort analysis of pancreatic cancer, 1939-69. *Cancer* 1977;**39**:1260-3.
- Stocks P. Cancer mortality in relation to national consumption of cigarettes, solid fuel, tea, and coffee. *Br J Cancer* 1970;**24**:215-25.
- Lin RS, Kessler II. A multifactorial model for pancreatic cancer in man—epidemiological evidence. *JAMA* 1981;**245**:147-52.
- MacMahon B, Yen S, Trichopoulos D, Warren K, Nardi G. Coffee and cancer of the pancreas. *N Engl J Med* 1981;**304**:630-3.
- Department of International Economic and Social Affairs, Statistical Office. *Demographic yearbook—historical supplement*. Special Issue. New York: United Nations, 1979.
- US Department of Commerce. *Population estimates and projections: estimates of the population of the United States, by age, race, and sex*. Series P-25. Washington: US Department of Commerce, 1980.
- Devesa SS, Silverman DT. Cancer incidence and mortality trends in the United States: 1935-74. *J Natl Cancer Inst* 1978;**60**:545-71.
- Segi M, Kurihara M. *Cancer mortality for selected sites in 24 countries*. No 6. Department of Public Health, Tohoku University. Japan Cancer Society, 1972.
- Podolsky DK, McPhee MS, Alpert E, Warshaw AL, Isselbacher KJ. Galactosyltransferase isoenzyme II in the detection of pancreatic cancer: comparison with radiologic, endoscopic, and serologic tests. *N Engl J Med* 1981;**304**:1313-8.
- Hermann RE, Cooperman AM. Current concepts in cancer: cancer of the pancreas. *N Engl J Med* 1979;**301**:482-5.
- Reed K, Vose PC, Jarstfer BS. Pancreatic cancer: 30 Year Review (1947 to 1977). *Am J Surg* 1979;**138**:929-33.
- Morgan RG, Wormsley KG. Progress report: cancer of the pancreas. *Gut* 1977;**18**:580-96.
- International Coffee Organisation. *A report on coffee drinking in the United States, winter 1980*. London: ICO, 1980. (Study performed by Data Group, Inc, Elkins Park, Pa.)
- Waterhouse J, Muir C, Correa P, Powell J. *Cancer incidence in five continents*. Vol III. IARC Scientific Publications No 15. Lyon: International Agency for Research on Cancer, 1976.
- Glantz SA. *Primer of biostatistics*. New York: McGraw-Hill Book Company, 1981;326.
- Surgeon General. *Smoking and health*. Washington: DHEW, 1979. (DHEW Publication No (PHS) 79-50066, 5-50 to 5-53.)
- Doll R, Peto R. Mortality in relation to smoking: 20 years' observations on male British doctors. *Br Med J* 1976;**iii**:1525-36.
- Doll R, Gray R, Hafner B, Peto R. Mortality in relation to smoking: 22 years' observations on female British doctors. *Br Med J* 1980;**280**:967-71.
- Weiss W. Epidemiology and etiology. In: Greco A, Oldham R, Bunn PA, eds. *Small cell lung cancer*. Chap 1. New York: Grune and Stratton, Inc, 1981.
- Surgeon General. *Smoking and health*. Washington: DHEW, 1979. (DHEW Publication No (PHS) 79-50066, A-15.)
- Mancuso TF, El-Attar AA. Cohort study of workers exposed to beta-naphthylamine and benzidine. *JOM* 1967;**9**:277-85.
- Li FP, Fraumeni JF, Mantel N, Miller RW. Cancer mortality among chemists. *J Natl Cancer Inst* 1969;**43**:1159-63.
- Sparks PJ, Wegman DH. Cause of death among jewelry workers. *JOM* 1980;**22**:733-6.
- Friedman GD, Siegel AB, Seltzer CC. Cigarette smoking and exposure to occupational hazards. *Am J Epidemiol* 1973;**98**:175-83.

(Accepted 20 November 1981)