Cardiovascular and other causes of death as a function of lifestyle habits in a quasi extinct middle-aged male population. A 50-year follow-up study

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ABSTRACT

Objectives: To relate major causes of death with lifestyle habits in an almost extinct male middle-aged population.
Material and methods: A 40–59 aged male population of 1712 subjects was examined and followed-up for 50 years. Baseline smoking habits, working physical activity and dietary habits were related to 50 years mortality subdivided into 12 simple and 3 composite causes of death by Cox proportional hazard models. Duration of survival was related to the same characteristics by a multiple linear regression model.
Results: Death rate in 50 years was of 97.5%. Out of 12 simple groups of causes of death, 6 were related to smoking habits, 3 to physical activity and 4 to dietary habits. Among composite groups of causes of death, hazard ratios (and their 95% confidence limits) of never smokers versus smokers were 0.68 (0.57–0.81) for major cardiovascular diseases; 0.65 (0.52–0.81) for all cancers; and 0.72 (0.64–0.81) for all-cause deaths. Hazard ratios of vigorous physical activity at work versus sedentary physical activity were 0.63 (0.49–0.80) for major cardiovascular diseases; 1.01 (0.72–1.41) for all cancers; and 0.76 (0.64–0.90) for all-cause deaths. Hazard ratios of Mediterranean Diet versus non-Mediterranean Diet were 0.68 (0.54–0.86) for major cardiovascular diseases; 0.54 (0.40–0.73) for all cancers; and 0.67 (0.57–0.78) for all-cause deaths. Expectancy of life was 12 years longer for men with the 3 best behaviors than for those with the 3 worst behaviors.
Conclusions: Some lifestyle habits are strongly related to lifetime mortality.

1. Introduction

The combined role of some lifestyle behaviors, such as cigarette smoking, physical activity and eating habits, as determinants of coronary heart disease, cardiovascular diseases, cancer and all-cause mortality has been documented by many reports based on population studies [1–16]. These observations, apart some rare exceptions [14] covered relatively short follow-up periods, usually less than 25 years.

Some population studies that started in the mid of the last century have reached very long observation periods coming to the quasi-extinction of the original cohorts [17–19]. This allows to tackle systematically the problem by considering several groups of causes of death that represent the outcome of a life-long experience.

The Italian Rural Areas of the Seven Countries Study of Cardiovascular Diseases enrolled in 1960, have reached 50 years of follow-up with complete data on mortality and causes of death and an overall death rate of 97.5% [18,20]. The purpose of this analysis is to study the relationships of 3 lifestyle behaviors, that is cigarette smoking, physical activity and dietary habits, with several groups of causes of death that may roughly be considered of different etiology. The null hypothesis is that those lifestyle characteristics have no relationship with the various causes of death.

2. Material and methods

2.1. Population and measurements

The epidemiological material used for this analysis derives from the Italian Rural Areas of the Seven Countries Study of Cardiovascular Diseases, made of 1712 middle-aged (40 to 59 years) men at entry examination in 1960, representing 98.5% of defined samples. More details can be found elsewhere [18,20].

We considered 3 lifestyle behaviors as follows: *a*) Cigarette smoking was evaluated by a questionnaire and 3 classes of smoking habits were used for analysis: never smokers, ex-smokers and current smokers (reference for multivariate analysis); *b*) Physical activity was derived

from a questionnaire that matched some simple questions with the profession. Then, 3 levels of physical activity at work were defined, i.e. sedentary (reference for the multivariate analysis), moderate and vigorous. The mean energy expenditure of these 3 levels was roughly estimated by a parallel study where ergonometric measurements were taken [21] and independently by the caloric intake measured on the diet [22]. The means of these estimates are reported in Table 1; *c*) Dietary habits were measured using the dietary history [22] and the outcome was converted into 18 food groups. Factor analysis was carried out and one of the 3 explored factors (factor 2) was chosen to produce factor score estimates for each subject. Details on the procedure are reported elsewhere [23]. Factor score is the score, for each case computed by exploiting the factor score coefficients, i.e. the estimate for a case of an underlying factor formed from the linear combination of the observed variables. This means that each factor becomes a numerical characteristic of each individual that can be used as a variable in subsequent modeling.

Since the questionnaires were administered a few years after the baseline examination, factor scores were regressed on age to reach the entry baseline value, while for 25% of subjects with missing data it was imputed by multivariate normal procedure by using as reference 30 other personal characteristics [20]. No significant difference was found between the mean of the original values and that of the imputed values. Moreover, Cox models for the prediction of events with and without the imputed values of factor score produced similar coefficients for the dietary indices. Factor score is a continuous variable that can be used as such or divided in sections to identify groups with different characteristics. Therefore it was divided in quintiles and, arbitrarily, quintile 1 was called non-Mediterranean Diet (reference for the multivariate analysis), quintiles 2, 3 and 4 were called Prudent Diet, and quintile 5 was called Mediterranean Diet. The term Prudent Diet was assigned to the intermediate category after the end of the analysis when it was shown that it was beneficial versus the one called non-Mediterranean Diet. In the original factor analysis the group arbitrarily called Mediterranean Diet was characterized by a definitely higher consumption, compared to the non-Mediterranean Diet class, of bread, cereals, potatoes, vegetables, fish, olive oil and lower consumption of sugar and milk, while this was true, for the Prudent Diet group, to a lesser extent.

Systematic collection of mortality data including date and causes of death was performed for 50 years and was based (beyond the death certificates) for at least half of cases on a procedure that anticipated the structure and the concepts of the so called verbal autopsy [24]. Cases of death were coded following the 8th Revision of the WHO-ICD [25] and were allocated by a single reviewer (AM), following defined criteria. In the presence of multiple causes (recorded in more than half of cases) and in case of serious doubts about the correct major cause of death, a hierarchical rank was adopted for re-classifying the order of causes of death with violence, cancer, coronary heart disease (CHD), stroke and other causes in sequence.

Using the first re-classified cause of death, 12 groups of causes of death were created, partly reflecting the structure of the international classification, partly making arbitrary choices bound to the magnitude of groups and convenience. Some groups were then added together to produce larger groups and finally also all-cause deaths were computed. Altogether 15 groups were analyzed.

Collection of data started well before the era of the Helsinki Declaration, with consent implied by participation in the examinations, while at 5-year follow-up survey verbal consent was obtained to collect follow-up data.

2.2. Statistical analysis

Death rates of the various groups of simple and composite causes of death were computed from the 50-year follow-up mortality data. Cox proportional hazard models were solved with each cause of death as end-point and the 3 lifestyle behaviors as covariates each divided into the 3 classes described above, and age. Kaplan–Meier survival curves related to all-cause mortality as a function of 3 behaviors were computed for the production of figures.

A multiple linear regression model was solved using the years lived after entry examination as dependent variable (survival) and the 3 behaviors divided into the 3 classes as independent variables.

3. Results

Table 1 summarizes the behavioral habits of the study population, as described above. They reflect the situation of men living in rural communities in the mid of the last century, with a relatively high prevalence of current smokers, high mean levels of physical activity bound to work, and varied dietary habits, still oriented in prevalence toward healthy habits.

In 50 years, 1669 men died out of the 1712 enrolled at entry (97.5%) which corresponds to the almost extinction of the cohort. None of the baseline examined subjects was lost to follow-up. The most common (simple) causes of death were other (than lung) cancers (23.0%), followed by coronary heart disease (19.1%) and stroke (13.5%). When composite groups were considered, major cardiovascular diseases (of arteriosclerotic-hypertensive origin) were the dominant causes (43.7%), followed by all cancers (27.6%), the sum of the two reaching 70% of all deaths.

Cox proportional hazard models for each of the groups of causes of death are reported in detail in Appendix 1. An easier readable summary is given in Table 2, with hazard ratios of never smokers/current smokers; physically vigorous/physically sedentary (related to work); and Mediterranean Diet/non-Mediterranean Diet.

Smoking habits showed a significant relationship in 6 simple groups of causes of death, that is coronary heart disease, heart disease of uncertain etiology, stroke, lung cancer, chronic bronchitis, cause unknown, and with cardiovascular diseases, cancer and all causes among

Table 1
Lifestyle behavior habits in the study population.

Behavior	Method	Classes and proportions	Notes
Cigarette smoking	Standard questionnaire	1. Never smokers 25.4% 2. Ex-smokers 13.6% 3. Current smokers 61.0%	
Physical activity	Standard questionnaire matched with working activity	1. Sedentary 9.7% 2. Moderate 22.1% 3. Vigorous 68.2%	Mean estimated energy expenditure Sedentary 2500 kcal Moderate 2700 kcal Vigorous 3100 kcal
Dietary habits	Dietary history	1. Non-Mediterranean 19.6% 2. Prudent 60.2% 3. Mediterranean 20.2%	Derived from factor score of factor analysis, divided in quintile classes and taken as 1 = quintile 1 2 = quintile 2,3,4 3 = quintile 5