Role of modifiable risk factors in life expectancy in the elderly

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Objective The aim of the present study was to evaluate the role of 'modifiable' risk factors, assessed between the ages of 60 and 70 years, in late survival.

Design The study population included subjects aged 60–70 years, who had a standard health examination at the IPC Center, and who could potentially reach the age of 80 years for men and 85 years for women at the end of the follow-up period.

Methods The role of 'modifiable' risk factors was assessed by comparing subjects who died before the age of 80 years for men ($n = 1333$) and before 85 years for women ($n = 543$) to subjects who survived beyond these ages (3681 men, 1910 women). Multivariate analyses were conducted to determine which parameters were independently associated with survival to an advanced age.

Results The multivariate analysis showed a decreased probability of late survival with higher pulse pressure ($P < 0.0001$), higher heart rate ($P < 0.002$), higher glycemia ($P < 0.0034$), and an increased probability with regular physical activity ($P < 0.0001$). A significant interaction between heart rate and gender ($P < 0.01$) was observed, indicating that heart rate was a predictor of late survival in men but not in women. Body mass index, cholesterol and triglyceride levels, and diastolic blood pressure and tobacco smoking were not associated with late survival in this population.

Conclusions A systematic search for certain risk factors in an elderly patient can have a significant impact on late survival and can lead to the establishment of priority goals, such as increasing physical activity and reducing blood pressure, heart rate and glycemia. *J Hypertens* 23:1803–1808 © 2005 Lippincott Williams & Wilkins.

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Introduction

Preventive medicine has developed considerably in the recent years. Assessment of factors with a predictive value for morbidity and mortality has become a major issue which has considerable medical, social and economic consequences. This concept, which evolved primarily in the field of cardiovascular medicine, led to the creation of a large number of risk evaluation equations. However, most of these equations are based on data obtained from middle-aged populations [1–3].

The ageing of the population in industrialized countries, and the consequent increase in preventive medicine among the elderly, raises the following pertinent questions: do risk factors play the same role in older subjects? Which parameters should be tested in the elderly in order to evaluate risk? Can factors associated with longevity be identified?

The aim of the present study was to evaluate the predictive value of clinical and biological parameters assessed in subjects aged 60–70 years of age, in the survival to 80 years for men and 85 years for women (which corresponds to the mean life expectancy at these ages in men and women, respectively). We included individuals who had a health examination at the Centre d'Investigations Préventives et Cliniques (IPC Center) at the age of 60–70 years and who, at the end of the study's follow-up period, had the potential to reach the age of 80 years for men and 85 years for women.

Methods

The IPC population

Subjects were examined at the IPC Center. This medical center, which is subsidized by the French national health care system (Sécurité Sociale-CNAM), provides all working and retired persons and their families with a free medical examination every 5 years. It is one of the largest medical centers of this kind in France, having carried out approximately 20 000–25 000 examinations per year since 1970 for people living in the Paris area.

In the present study we evaluated the impact of nine 'modifiable' parameters on survival to an advanced age. These parameters included five classical major cardiovascular risk factors – blood pressure [systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse pressure (PP)], total cholesterol, glycemia, tobacco smoking and electrocardiographic left ventricular hypertrophy (LVH) – and four factors which are potentially implicated in morbidity and mortality – body mass index (BMI), triglycerides, heart rate (HR) and physical activity. Personal history of disease and age were considered for statistical adjustments. Forced expiratory volume (FEV) ratio was also measured as a global indicator of health and introduced in the multivariate logistic analyses as a covariate.

Supine blood pressure was measured three times in the right arm, after a 10-min rest period, using a manual sphygmomanometer. The mean of the last two measurements was calculated. HR was measured by electrocardiogram (ECG) after a 5- to 7-min rest period and was subsequently entered into the database as a categorical value (4 classes: <60, 60–80, 81–100, >100 bpm) and not as a continuous value. For the purpose of the present study, subjects were divided into two HR groups: HR $\leq$ 80 bpm and HR > 80 bpm. Data pertaining to physical activity were obtained from a self-administered questionnaire. Subjects who declared having a regular physical activity, that is more than 2 h/week, were considered as physically active. Tobacco use (current consumption of more than 10 cigarettes/day) and personal and family history of heart disease were also obtained from the self-administered questionnaire. Biological parameters (total cholesterol, triglycerides) were measured at the IPC Center under fasting conditions, at the time of the examination. Glycemia was measured 2 h after absorption of 75 g of glucose. FEV ratio was measured with a Spyro Analyser spirometer (Model ST-200; Fukuda Sangyo) and calculated as the ratio between measured FEV/theoretical FEV.

The IPC Center received authorization from the Comité National d'Informatique et des Libertés (CNIL) to conduct these analyses. Vital status, for the period extending from the time of study inclusion through December 1997 (mean follow-up 18 years), was obtained for the entire study population. These data were obtained from the mortality records at the 'Institut National de Statistiques et d'Etudes Economiques' (INSEE), following a previously established procedure [4]. In order to validate the procedure, we took a random sample of 250 subjects and compared our data with those found in city hall registries. A discordance was found in only two cases (<1%), enabling us to consider that we had a complete follow-up for the entire study population.

All subjects included in this analysis gave their informed consent at the time of the examination. The description of the IPC cohort has been detailed previously [4].

In the present analysis, we included subjects based on the following criteria: (1) examined at the IPC Center between 1972 and 1981; (2) aged 60–70 years at the time of the examination; and (3) with the potential to reach the age of 80 years for men and 85 years for women by December 1997, based on age at the time of the examination and the follow-up period.

All individuals who met these criteria were included in the present analysis. The following two groups were established: alive subjects, which included 3681 men who were still alive after 80 years of age and 1910 women who were still alive after 85 years of age, and deceased subjects, which included 1333 men who died before reaching the age of 80 years and 543 women who died before reaching 85 years of age. A total of 5014 men and 2453 women were included.

Data analysis

Differences in the modifiable risk factors between survivors and subjects who died before the age of 80 or 85 years for men and women, respectively, were examined. Analyses of variance, adjusted for age, were used to compare the groups of deceased and alive subjects. To identify determinants of survival probability, multivariate logistic regression analyses were carried out including the nine modifiable risk factors in addition to non-modifiable parameters (age, gender, personal history of diseases, expiratory volume ratio). Survival probability was calculated according to the number of modifiable risk factors. The following factors were considered: absence of physical activity, heart rate > 80 bpm, glycemia > 2.0 g/l (11 mmol/l) and pulse pressure $\geq$ 65 mmHg.

All statistical analyses were carried out using the SAS (8.02) statistical software package (SAS Institute Inc., Cary, North Carolina, USA).

Results

Univariate analyses

Mean age ($\pm$SD) at the time of the examination was 65.3 ± 2.8 years. Table 1 shows clinical and biological parameters according to vital status. After adjustment for age, subjects who were alive after the age of 80 years for men and 85 years for women, as compared to those who died prior to that age, presented lower levels of blood pressure, HR, BMI and glycemia, and higher levels of physical activity. No difference between the two groups was observed for total cholesterol, triglycerides, cigarette smoking and the presence of left ventricular hypertrophy on ECG. These findings were present in both men and women, with the exception of HR which was different in

Table 1 Age-adjusted values for clinical and biological parameters in men and women aged 60–70 years at the time of study inclusion, according to vital status at 80 years for men and 85 years for women

	Men		Women		All	
	Deceased	Alive	Deceased	Alive	Deceased	Alive
n	1333	3681	543	1910	1876	5591
Age (years)	64.6 (2.9)	65.0 (2.9)	65.9 (2.5)	66.1 (2.4)	65.0 (2.8)	65.3 (2.8)
Body mass index (kg/m^2)	25.9 (0.09)	25.6 (0.05)**	24.9 (0.2)	24.5 (0.09)*	25.6 (0.08)	25.3 (0.05)**
Systolic blood pressure (mmHg)	155.0 (0.6)	148.7 (0.4)***	154.2 (1.0)	147.7 (0.5)***	154.7 (0.5)	148.4 (0.3)***
Diastolic blood pressure (mmHg)	92.2 (0.4)	89.6 (0.2)***	89.8 (0.5)	86.8 (0.3)***	91.4 (0.3)	88.7 (0.2)***
Pulse pressure (mmHg)	62.8 (0.4)	59.1 (0.3)***	64.3 (0.6)	60.9 (0.3)***	63.3 (0.3)	59.7 (0.2)***
Heart rate (% of subjects >80 bpm)	25.9	16.9***	32.2	30.7	27.6	21.1***
Left ventricular hypertrophy (%)	1.35	0.87	0.74	0.58	1.2	0.8
Cholesterol (g/l)	2.25 (0.01)	2.26 (0.06)	2.50 (0.02)	2.46 (0.01)*	2.33 (0.01)	2.33 (0.005)
Glycemia (g/l)[a]	1.80 (0.01)	1.75 (0.008)**	1.87 (0.02)	1.81 (0.01)**	1.83 (0.01)	1.77 (0.006)***
Triglycerides (g/l)	1.45 (0.05)	1.41 (0.03)	1.30 (0.07)	1.20 (0.04)	1.43 (0.04)	1.37 (0.02)
Physical activity (%)	19.6	28.2***	10.5	14.0*	17.0	23.3***
Tobacco (%)	16.7	19.0	3.0	2.8	12.9	13.5

[a]Glycemia 2 h after absorption of 75 g glucose. Deceased versus alive: *$P < 0.05$; **$P < 0.001$; ***$P < 0.0001$.

men but not in women according to the vital status. Also, women who died prior to 85 years had slightly higher cholesterol levels. No such difference was observed in men.

Multivariate logistic regression analyses

After adjustment for age, gender, personal history of cardiovascular disease and forced expiratory volume ratio, multivariate logistic regression analyses were conducted in order to determine the independent roles played by the different 'modifiable' risk factors in the probability of survival to an advanced age (beyond 80 years of age for men and beyond 85 years for women). The results of this analysis (Table 2) showed that PP, HR, physical activity and glycemia were the four independent 'modifiable' risk factors that influenced the probability of late survival.

Following the analysis presented in Table 2, an increase of 10 mmHg of PP led to an 11% decrease in the probability of late survival ($P < 0.0001$), and the presence of a high heart rate (>80 bpm) led to a 23% decrease in the probability of late survival ($P < 0.002$). Subjects who had regular physical activity had a 52% increased probability of late survival ($P < 0.0001$). Finally, increased postprandial glycemia significantly reduced the probability of late survival ($P < 0.0034$) though this effect was clinically less important (+1 mmol of glycemia led to a 4% decrease in the probability of late survival). BMI, cholesterol and triglyceride levels, DBP and tobacco smoking were not associated with late survival in this population.

Table 2 Multivariate logistic regression analyses including the significant 'modifiable' risk factors for survival to an advanced age

	Odds ratio (95% CI)	χ^2	*P*
All			
Pulse pressure (10 mmHg)	0.89 (0.84–0.93)	22.3	0.0001
Glycemia (1 mmol/l)[a]	0.96 (0.93–0.99)	8.6	0.0034
Physical activity (Yes/No)	1.52 (1.27–1.83)	20.7	0.0001
Heart rate (>80 bpm)	0.77 (0.66–0.91)	9.8	0.002

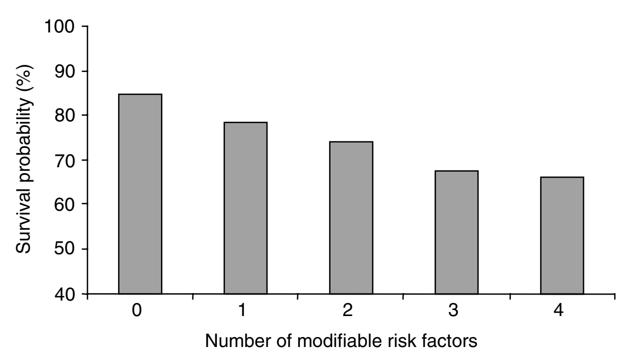
[a]Glycemia 2 h after absorption of 75 g glucose. After adjustment for age, gender, personal history of cardiovascular disease and forced expiratory volume. CI, confidence interval.

SBP and DBP were also significant determinants (when put into the model separately instead of PP) but were less powerful than PP. Finally, when SBP and DBP were introduced simultaneously into the model, SBP but not DBP was statistically significant.

A significant interaction ($P < 0.01$) was observed between HR and gender on late survival. A separate multivariate analysis in men and women showed that HR was a significant determinant in men but not in women. Men with a heart rate > 80 bpm had a 20% lower probability of surviving after the age of 80 years (odds ratio 0.80, 95% confidence interval 0.69–0.90, $P < 0.005$) as compared to men with a heart rate $\leq$ 80 bpm. No such interaction was found for the other parameters studied.

Based on multivariate analyses, Figure 1 presents the survival probability for the study population as a whole

Fig. 1



Survival probability (%) to 80 years of age in men and 85 years of age in women, according to the presence of 'modifiable' risk factors (pulse pressure, heart rate, physical activity, glycemia) at the age of 60–70 years.

according the number of modifiable risk factors that were found to be significant determinants of survival [absence of physical activity, HR > 80 bpm, glycemia > 2.0 g/l (11 mmo/l) and PP ≥ 65 mmHg]. Survival probability was 84.6% in the absence of risk factors, and dropped to 78.5, 74.0, 67.5, 66.2% in the presence of 1, 2, 3 and 4 'modifiable' risk factors, respectively.

Discussion

The present report demonstrates the importance of evaluating several risk factors in the elderly, factors that play an important role in the estimation of the probability of reaching a very advanced age. The accumulation of high PP, high HR and high glycemia, and the absence of regular physical activity, dramatically decrease the probability of late survival from 84.6 to 66.2%. This report also demonstrates important changes in the role of certain major classical risk factors found among younger people, which no longer seem to have the same impact in the elderly. Among major modifiable risk factors, low PP, low HR, low postprandial glycemic levels and physical activity, were independent predictors of survival to an advanced age. DBP, tobacco smoking and total cholesterol were not associated with late survival.

Hemodynamic factors

Blood pressure

It has been reported previously that in younger subjects both SBP and DBP are strong determinants of cardiovascular disease (CVD) risk, whereas with advanced age most studies have shown that SBP and PP better reflect CVD risk than DBP [5–12]. DBP levels are influenced by arterial and arteriolar alterations in opposite ways: an increase in peripheral vascular resistance leads to an elevation in DBP, whereas stiffening of large arteries can contribute to a decrease in DBP [11,12]. Arterial stiffness occurs with aging, primarily after the sixth decade, leading to a decrease in DBP and a concomitant increase in SBP and PP. Since arterial stiffness is associated with increased risk, low DBP can be associated with higher mortality risk. These hemodynamic considerations may explain why the predictive role of DBP decreases with age. On the other hand, the roles of SBP and PP increase with age since they reflect primarily the degree of arterial stiffening [11,12]. Moreover, in older subjects, SBP measured at the brachial artery is a good indicator of central aortic pressure, whereas in younger subjects peripheral SBP overestimates central aortic pressure [12]. These hemodynamic considerations can also explain the recommendations found in the latest JNC guidelines suggesting that 'in persons older than 50 years SBP is a much more important cardiovascular risk factor than DBP' [13]. The present study indicates that among the different BP levels, PP evaluated in the elderly is the most powerful predictor of longevity.

Heart rate

This study provides evidence that HR recorded in the elderly has a strong predictive value in survival to an advanced age in men but not in women. An analysis of the Framingham study in middle-aged individuals showed that HR was positively associated with survival to 75 years of age [14]. A number of previous studies in younger subjects have shown the association between HR and all-cause and cardiovascular mortality was weaker or even absent in women [15–17]. Several hypotheses may explain this gender difference. It has been suggested that the mechanisms for elevated HR can differ among men and women [18]. It has also been suggested that pre-menopausal women, due to their hormonal status, are protected from the 'deleterious' effects of elevated HR. Although the present study cannot provide explanations for these gender-related differences, these results, as well as those in another report we recently published [19], show that even in post-menopausal women, unlike in men of the same age, HR is not associated with late survival.

Metabolic parameters and overweight

Total cholesterol

In the present analysis, cholesterol levels evaluated in the elderly were not significant determinants of survival to a very old age. The present results corroborate with some [20] but not all [21] previous reports showing a significant decrease in the role of total cholesterol in older subjects. There are a number of possible explanations for this. Early excessive mortality in subjects with dyslipidemia could be a primary explanation for the lack of predictive value of these risk factors in the elderly. Furthermore, age-related co-morbidity such as cancer and alcoholism could decrease cholesterol levels and 'mask' the deleterious effects of high cholesterol on longevity [22]. However, in the present study, the absence of any association between cholesterol levels and survival persisted after adjustment for alcohol consumption (data not shown) and after excluding subjects who died within the first 2 years of the follow-up period. These results cannot exclude the hypothesis that lipid fractions [low- and high-density lipoprotein (LDL and HDL), etc.], which were not measured in our population, are significantly associated with mortality and late survival. Moreover, these results cannot predict the possible benefits of hypolipemic treatments, especially with statins, in high-risk elderly subjects.

Hyperglycemia and overweight

The present study shows that glycemia measured in the elderly is a statistically significant determinant of late survival. It is important to note that in this cohort, post-prandial rather than fasting glycemia was measured. Therefore, the present study cannot answer the question as to whether or not glycemia measured under fasting conditions plays a stronger predictive role than postprandial glycemia.

Subjects who died before the age of 80 and 85 years in men and women, respectively, had significantly higher BMI. However, this difference was not significant after adjustment for the other risk factors. These results are in concordance with observations made in middle-aged populations [23,24]. However, overweight should be considered as an important risk factor since it is one of the major factors for developing hypertension and metabolic disorders in the elderly.

Lifestyle

Tobacco smoking

The absence of a significant influence of cigarette smoking on late survival in our population of elderly subjects may have several explanations. First, as we also mentioned for cholesterol, there is an increase in mortality in middle age among many smokers, especially heavy smokers. Second, heavy smokers are less likely to volunteer for this sort of health examination. Finally, we cannot disregard the possibility that a number of smokers did not declare their actual smoking habits when filling out the self-administered questionnaire, rendering the answers to those specific questions inaccurate.

Physical activity

The strong association between regular physical activity and late survival confirms results from several studies which showed a very significant implication of physical activity in the maintenance of several functions in the elderly [25]. One can consider that being physically active is the result, and not the cause, of a better health status and consequently survival to an advanced age. Although the present analysis cannot provide a definitive answer to this 'chicken and egg' relationship between longevity and physical exercise, the observed association was still highly significant after adjustment for age and several indicators of general health status, such as personal history of cardiovascular disease and expiratory volume, as well as associated risk factors. Therefore, we can suggest that the increased longevity observed in physically active subjects is not due to a better health status at the time of the study examination.

Clinical applications

The results of the present study confirm the importance of assessing several modifiable risk factors in order to estimate a patient's risk and probability for late survival. The study limitations are primarily related to the fact that this was an observational study and not a controlled interventional study. Therefore, we cannot really draw any solid conclusions as to the benefits in terms of longevity when 'correcting' these risk factors. Nevertheless, the results should incite physicians to provide their patients with explanations for the benefits of lowering SBP and PP, treating diabetes, and above all, the importance of regular physical exercise.

In conclusion, among elderly subjects, both high systolic and pulse pressure, lack of physical activity and high glycemia greatly reduce the probability of survival to an advanced age. High HR is also an independent predictor, but only in men. Establishing preventive measures to combat these risk factors could have a significant effect on life expectancy among the elderly.

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