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PREDICTORS OF MORTALITY IN VERY OLD SUBJECTS AGED 80 YEARS OR OVER

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We studied 318 subjects aged 80 years or over included in the Cardiovascular Study in the Elderly (CASTEL). Some well known risk factors (left ventricular hypertrophy, glucose intolerance, cholesterol, ApoB/ApoA ratio, triglycerides, proteinuria, cigarette smoking, and ECG abnormalities), whose importance in cardiovascular risk is definitely accepted for young adults, were very poor predictors of mortality in our survey. On the contrary, FEV_1 reduction and blood uric acid were strong predictors.

INTRODUCTION

A number of risk factors have been identified in young and middle-aged adults; many of them (hypertension, high blood cholesterol, cigarette smoking, diabetes) have an unquestionable relationship with cardiovascular mortality and morbidity.

The prevalence and importance of these risk factors in elderly subjects and their impact on mortality are practically unknown; in fact, age classes over 65 years have usually been excluded prior to both clinical and epidemiological trials.

In this study we evaluated, by means of logistic regression, the importance of some risk factors in predicting mortality in a cohort of very old subjects, aged 80 years or over.

MATERIALS AND METHODS

General protocol - This study is presented as a part of the *CASTEL* (Cardiovascular Study in the Elderly), an intervention prospective study performed in a town of northern Italy (Castelfranco Veneto, Treviso) (6). All subjects aged 65 years or over resident in Castelfranco Veneto (3088 subjects identified through the register's office) were invited to participate in the study; 2254 of them were enrolled, and 318 of them - aged 80 years or more - were considered "very old people" (VOPs).

Data collection - General data a and clinical history were collected by means of Rose's questionnaire (26). A fasting blood sample, a morning urine collection, a spyrometry, and a basal 12-lead electrocardiogram were also performed.

Blood pressure was measured by trained doctors using a Riva-Rocci sphygmomanometer in a sitting position. Systolic blood pressure was defined as the reading at the first Korotkow sound and diastolic as the reading at the last one (phase 5). In order to reduce the impact of the "alert reaction", blood pressure was taken 3 times: measurements followed each other at 10-minute intervals, and the average of the last 2 measurements was taken into consideration as "blood pressure" in this paper.

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Electrocardiograms were analysed on the basis of the Minnesota code (22, 26) by an expert who did not know the aim or design of the study.

Echocardiogram - A two-dimensional-guided monodimensional echocardiogram based on the recommendations of the American Society of Echocardiography (27) was performed in 55 subjects aged 80 years or more, and in 448 subjects aged less than 80, randomly chosen. The following left ventricular linear parameters were measured (in mm) from short-axis view (parasternal and long-axis views were also used when necessary): end-diastolic diameter (LVEDD), systolic diameter (LVSD), end-diastolic posterior wall thickness (LVEDPWT) and interventricular septum diastolic thickness (IVSDT). End-diastolic left ventricular volume (LVEDV, in ml) was calculated with the formula of Teicholz (32):

$$LVEDV = \frac{7\ LVEDD^3}{2.4 + LVEDD}$$

Left ventricular mass (*LVM*, in g) was calculated with the algorithm of Devereux (11):

$$LVM = 1.04\ [(IVSDT + LVEDD + LVEDPWT)^3 - LVDD^3] - 13.6$$

and left ventricular mass index (*LVMI*, in g/sm) by dividing LVM by body surface area (*BSA*, in sm) obtained by the formula of Du Bois and Du Bois (12):

$$BSA = weight^{0.425} \cdot height^{0.725} \cdot 71.84$$

Left atrial dimensions (LA, in mm) were also determined. Body mass index (BMI, in kg/m^2) was calculated from:

$$BMI = \frac{weight\ (kg)}{height^2\ (m)}$$

Vital status at the 7th year - The follow-up period lasted 7 years. Vital status was examined at the 7th year through the register's office. For subjects who died in hospitals, cause of death was confirmed through direct analysis of the hospital's case files. For those who died outside the hospital, the cause was confirmed with an analysis of the death medical certificate and by a questionnaire distributed to general practitioners.

Cut-off values - Hypertension was defined as a combination of elevated blood pressure values (systolic blood pressure $\geq$ 160 and/or diastolic blood pressure $\geq$ 95 mmHg), or a history of hypertension for people who were currently taking antihypertensive drugs.

According to Tunick *et al.* (33), the aortic root was considered normal when $<$ 40 mm, mildly dilated when ranging from 40 to 50 mm, and severely dilated when over 50 mm; the left atrium was considered normal when $<$ 40 mm, mildly dilated when ranging from 40 to 50 mm, moderately dilated when ranging from 51 to 59 mm and severely dilated when $\geq$ 60 mm; LVEDD was normal when $<$ 53 mm, mildly dilated when 53-60 mm, moderately dilated when 61-65 mm, and severely dilated when over 65 mm.

According to Hammond *et al.* (14), echocardiographic diagnosis of LVH was based on an LVMI $>$ 34 g/sm in men or $>$ 110 g/sm in women; the electrocardiographic diagnosis was based on the Minnesota Codes 3-1 or 3-3.

Diagnosis of left atrial enlargement was based on echocardiogram ($>$ 40 mm); that of atrial fibrillation or flutter on the Minnesota Code 8-3, that of myocardial ischemia on the Minnesota Codes 4-1 4-3, 5-1 5-3 if Codes 6-4, 7-1 and 7-2 were absent. Diagnosis of myocardial infarction required the Minnesota Code 1-1 or 1-2, being absent 6-4 and 7-1. See Table 5 for other codes.

Statistics - Comparisons between the mean values of different classes were performed by analysis of variance and of covariance, using the Tukey correction as post-hoc test. Bartlett's test was employed in order to compare two-category paired data. Standardised (adjusted) mortality ratios were calculated using the direct method (22). Backward stepwise logistic regression (likehood ratio method) including as independent variables age, sex, total and HDL-cholesterol, cigarette smoking, arterial hypertension, systolic and diastolic blood pressure, ECG abnormalities, serum uric acid, serum glucose, serum creatinine, FEV_1, body weight, BMI, echocardiographic and electrocardiographic LVH, clinical history of myocardial infarction, of *claudicatio intermittens*, and of stroke was employed in order to confirm the predictors of mortality.

RESULTS

Twenty-six cases were deleted because of lack of data. Mean age of the 318 elderly subjects aged 80 years or more (*VOPs*) was 83.0 $\pm$ 2.6 years, that of the 1910 subjects aged 65 to 79 years (old people: *OPs*) was 68.8 $\pm$ 13.3 years.

Prevalence of hypertension and average blood pressure values by age groups are summarised in Table 1.

Mean age at death was 87.4 $\pm$ 3.2 years among VOPs and 77.4 $\pm$ 4.0 years among OPs (p = 0.0001). The overall 7-year mortality rate was 25.2% (49.1% among VOPs and 21.3% among OPs); it was 55.7% in very old males and 46.1% in very old females (p = NS). Taking into consideration blood pressure values, mortality was 21.1% among normotensives (36.8% in VOPs and 18.5% in OPs, p = 0.001) and 27.3% among hypertensives (55.2% in VOPs and 22.7% in OPs, p = 0.0001). Table 2 shows mortality rates and

TABLE 1. - Mean ± SD of systolic (SBP) and diastolic (DBP) blood pressure and prevalence of hypertension and of isolated systolic hypertension (ISH) among the 318 *very old* subjects (VOPs).

Age	Number of subjects	SBP (mmHg)	DBP (mmHg)	Prevalence of hypertension (%)	Prevalence of ISH (%)
80-81	119	165.7 ± 26.7	89.6 ± 12.7	59.7	34.4
82-83	83	166.4 ± 22.7	90.5 ± 12.2	62.6	34.9
84-85	59	158.6 ± 29.7	86.6 ± 11.9	50.8	36.6
86-87	31	168.0 ± 28.7	89.9 ± 12.6	64.5	45.2
≥ 88	26	153.6 ± 17.2	81.8 ± 11.5	38.5	19.2

No statistical differences between age classes.

cardiovascular mortality in relation to blood pressure.

Prevalence of LVH diagnosed by echocardiogram in 504 subjects (ECHO-LVH) was 72.4%, and that of LVH diagnosed by Minnesota Code in 2225 subject (ECG-LVH) was 10.1% (see Table 3 for details and for prevalences in VOPs and OPs). The all-cause 7-year mortality rate was 53.6% among the 41 VOPs having an ECHO-LVH and 28.6% in the 14 without ECO-LVH (p = NS), and, respectively, 52.9% and 48.7% (p = NS) in the 34 with and in the 281 without ECG-LVH. By comparison, mortality was 22.7% among the 324 OPs having ECHO-LVH and 18.4% in the 125 without it (p = NS), and, respectively, 23.1% and 21.0% in the 191 with and in the 1719 without ECG-LVH (p = NS).

Echocardiographic left atrial dimensions were normal in 86.8% of VOPs and 85.7% of old people, mildly dilated in 11.9% and 13.1%, respectively, moderately dilated in 0.9% and 0.8% and severely dilated in 0.3% and 0.1%.

A moderate dilatation of aortic root was found in 1.9% of VOPs (all males) and 0.1% of OPs (81.1% males). The seven-year mortality rate was not different in VOPs having normal or dilated LVEDD (44.4% vs 59.1%, respectively, p = N.S.), normal or dilated left atrium (44.2% vs 53.6%, p = N.S.), normal or dilated aortic root (48.2% vs 50%, p = N.S.). Table 4 shows crude mortality by classes of left ventricle, left atrium and aortic dimensions. The standardised mortality ratio was 0.14 in subjects having a normal left atrium and 1.69 in those having a dilated left atrium. Logistic regression performed in the 55 VOPs and in the 448 OPs who underwent echocardiogram demonstrated that echocardiophic abnormalities (including LVH) did not play any role in determining mortality.

In Table 5, prevalence of electrocardiographic abnormalities and mortality in relation to them are summarised. Overall crude mortality was significantly higher in OPs having ischemia, right bundle branch block or atrial fibrillation than in those not having it, while no significant difference in mortality was observed among VOPs in relation to ECG abnormalities. Logistic regression demonstrated that atrial fibrillation was the only electrocardiographic abnormality which determined mortality among VOPs (ß = 0.0363, p = 0.0151), while among OPs necrosis and ischemia were also predictors of mortality (respectively: ß = 0.8315, p = 0.0021; ß = 0.3068, p = 0.0417).

Average total cholesterol of VOPs who subsequently died was lower than in those living at the seventh-year (215.9 ± 38.9 vs 225.3 ± 38.9 mg/dl, p = 0.0001). Both total cholesterol and triglycerides at the initial survey were higher in females than in males (p = 0.0001). All-cause 7-year overall mortality in relation to blood cholesterol and to ApoB/ApoA ratio in both VOPs and OPs is shown in Figure 1. Logistic regression demonstrated that HDL-cholesterol, ApoB, ApoA, and ApoB/ApoA ratio did not play any role in determining overall cardiovascular or cancer mortality among VOPs; total cholesterol was a predictor of overall and cardiovascular mortality in VOPs (ß = -0.0072, p = 0.035) but not in OPs. In particular, cholesterol did not predict cancer mortality (ß = 0.0318, p = 0.8585).

Prevalence of hypertension was not different between normoglycemic, borderline or diabetic VOPs. Neither LVMI nor ECHO-LVH were different between subjects having a normal or an impaired glucose tolerance. Crude mortality by glucose tolerance is shown in Figure 1. Logistic regression demonstrated that neither blood glycemia nor clinical history of diabetes were predictors of mortality among VOPs, although glycemia was a predictor among OPs (ß = 0.009, p = 0.0001).

Table 6 shows crude mortality in relation to 5 classes of FEV1 (< 20%, 20-39%, 40-59%, 60-79% and ≥ 80% of theoretical values). Logistic regression demonstrated that FEV1 was a predictor of mortality among both VOPs (ß = -0.0094, p = 0.0445) and OPs (ß = 0.0115, p = 0.0001).

Blood uric acid concentrations were higher in VOPs who subsequently died than in those still alive

TABLE 2. - 7-year cardiovascular overall (Tot) and cardiovascular (Card) crude mortality by systolic and diastolic blood pressure among the 318 very old subjects (VOPs) and, by comparison, among subjects aged 65 to 79 years (OPs).

Blood pressure (mmHg)	Mortality (%)					
	Males		Females		All	
	Very old subjects (VOPs)					
	Total	Card	Total	Card	Total	Card
	SYSTOLIC					
< 120	50.0	16.7	44.4	22.2	46.7	20.0
120-139	45.4	27.3	36.0	28.0	38.9	27.8
140-159	51.8	40.7	39.7	23.3	43.0	28.9
160-179	58.3	33.3	53.7	40.7	55.1	38.5
180-199	66.7	27.3	43.2	29.7	50.9	34.5
≥ 200	54.5	27.3	65.2	47.8	61.8	41.2
	DIASTOLIC					
< 50	-	-	-			-
50- 69	33.3	16.6	25.0	14.3	28.6	14.3
70- 89	58.0	36.0	40.5	27.0	46.0	29.8
90-109	51.5	33.3	54.0	40.2	53.3	38.3
110-129	75.0	33.3	53.3	26.7	60.9	65.2
≥ 130	-	-	-	-		-
	Old subjects (OPs)					
	Total	Card	Total	Card	Total	Card
	SYSTOLIC					
< 120	32.2	17.6	10.0	10.0	24.1	14.8
120-139	19.7	11.8	22.3	12.9	21.2	12.4
140-159	25.8	14.0	15.7	8.3	20.1	10.7
160-179	34.7	15.0	15.5	9.6	22.5	11.6
180-199	30.8	17.0	16.7	10.4	21.3	12.6
≥ 200	20.0	15.5	21.6	11.7	21.1	12.8
	DIASTOLIC					
< 50	-	-	-			-
50- 69	33.3	16.6	25.0	14.3	28.6	14.3
70- 89	58.0	36.0	40.5	27.0	46.0	29.8
90-109	51.5	33.3	54.0	40.2	53.3	38.3
110-129	75.0	33.3	53.3	26.7	60.9	65.2
≥ 130	-	-	-	-		-

No statistical differences between classes of blood pressure.

TABLE 3. - Prevalence (%) of left ventricular hypertrophy diagnosed by echocardiogram (LVMI > 134 g/sm in men, > 110 g/sm in women) and by Minnesota Code (3-1, 3-3), in males (M) and females (F). Number of subjects in brackets.

Age (yrs)		Normotensives			Hypertensives			All		
		M	F	All	M	F	All	M	F	All
≥ 80	ECHO	25.0$ (4)	100.0 (3)	57.1 (7)	58.8$ (17)	87.1 (31)	77.1 (48)	52.4$ (21)	88.7 (34)	75.9 (55)
	ECG	14.3 (35)	4.2 (71)	7.5 (106)	14.5 (62)	13.4 (147)	12.4 (209)	14.4 (97)	9.2 (218)	10.8 (315)
65-79	ECHO	40.5$* (37)	75.7* (37)	58.1 (74)	57.6$$ (132)	84.3 (242)	74.9 (374)	53.8$$ (169)	61.3 (279)	72.2 (448)
	ECG	7.1 (310)	7.3 (355)	7.2 (665)	14.7 (436)	9.8 (809)	12.5 (1245)	11.5 (746)	9.0 (1164)	10.0 (1910)

Chi-square: $p = 0.004, $$p = 0.0001 vs F; *p = 0.0001 vs hypertensives.
No significant differences between VOPs and OPs.

TABLE 4. - All-cause and cardiovascular 7-year mortality by left atrium diameter (LA), left ventricular end-diastolic diameter (LVEDD) and aortic root diameter (AORTA).

LA (mm)	age classes ≥ 80	age classes 65-79	LVEDD (mm)	age classes ≥ 80	age classes 65-79	AORTA (mm)	age classes ≥ 80	age classes 65-79
				Total mortality (%)				
< 40	44.2	16.4	< 53	44.4	17.1	< 40	48.1	17.8
40-50	50.0	20.1	53-59	75.0	18.9	40-50	50.0	22.3
51-59	66.6	25.0	60-64	0.0	29.2	> 50	-	0.0
≥ 60	100.0	50.0	≥ 65	50.0	15.4			
				Cardiovascular mortality (%)				
< 4	8.6	30.9*	< 53	33.3	10.6	< 40	32.7	0
40-50	9.8	35.5*	53-59	50.0	22.9	40-50	33.3	15.1
51-59	26.7	40.0	60-64	50.0	9.4	> 50	-	11.7
≥ 60	33.3	100	≥ 65	0.0	7.7			

Chi-square: *p = 0.0001 vs ≥ 80 years.

TABLE 5. - All-cause and cardiovascular 7-year mortality in very old subjects (VOPs) and in those ranging 65 to 79 years of age (OPs), after dividing subjects into those with electrocardiographic abnormality present (Pr) or absent (Ab). Abnormalities are listed in order of total prevalence in the total population. LAH: left-anterior hemiblock, RBBB: right bundle branch block, AVB: atrio-ventricular block, LBBB: left bundle branch block, AF: atrial fibrillation, LPH: left posterior hemiblock.

	Minnesota Codes	Total prevalence (n = 2254)	Mortality rates Age ≥ 80 yrs		Age 65-79 yrs	
			Present	Absent	Present	Absent
		Total mortality (%)				
Ischemia	(4-1, 4-3, 5-1, 5-3)	23.9	49.1	49.3	29.7	18.9***
LAH	(2-1)	13.0	45.9	50.0	24.0	20.9
RBBB	(7-2, 7-3, 7-5)	7.5	50.0	49.1	33.6	20.4**
AF	(8-3)	4.0	52.9	49.0	35.6	20.7*
AVB	(6-3)	3.9	59.1	48.5	22.7	21.2
LBBB	(7-1, 7-6)	3.9	66.7	47.9	32.8	20.9
LPH	(2-2, 2-3)	0.4	66.7	49.0	35.6	20.7
		Cardiovascular mortality (%)				
Ischemia	(4-1, 4-3, 5-1, 5-3)	23.9	31.0	35.7	9.6	19.2***
LAH	(2-1)	13.0	33.1	31.1	11.5	13.5
RBBB	(7-2, 7-3, 7-5)	7.5	33.1	30.0	11.5	14.8
AF	(8-3)	4.0	31.9	47.0	11.1	0.0***
AV	(6-3)	3.9	32.7	0.0	11.7	0.0
LBBB	(7-1, 7-6)	3.9	32.0	42.8	11.3	22.4***
LPH	(2-2, 2-3)	0.4	33.0	0.0	11.7	0.0

Chi-square: *p = 0.009, **p = 0.002, ***p = 0.0001 vs Present.

at the seventh year (6.1 ± 1.7 vs 5.3 ± 1.5 mg/dl, p = 0.0001); a similar relationship was observed in OPs (5.7 ± 1.6 vs 5.3 ± 1.4 mg/dl, p = 0.002). The relationship between mortality and blood uric acid level (Fig. 1) was independent of age (Winer's test: F-ratio = 0.003, p = 0.587; ANOCOVA with age as covariate: F-ratio = 9.431, p = 0.002) and of systolic blood pressure (Winer's test: F-ratio = 5.674, p = 0.917; ANOCOVA with systolic as covariate: F-ratio = 9.431, p = 0.066), for this reason, no corrections for age or blood pressure were made. Logistic regression showed that blood uric acid was a predictor of mortality among both VOPs (ß = 0.275, p = 0.0041) and OPs (ß = 0.1486, p = 0.0011).

TABLE 6. - All-cause and cardiovascular 7-year mortality by reduction of FEV_1 (first column indicates % of the theoretical values).

	Age ≥ 80 years			Age 65 to 79 years		
	Males	Females	All	Males	Females	All
			Total mortality			
< 20	75.0	56.4	59.4	44.4	46.0	45.5
20-39	66.7	58.3	60.0	39.0	30.0	34.1
40-59	63.1	66.7	65.3	35.6	21.8	27.2
60-79	50.0	31.1	35.1	31.9	16.7	22.1
≥ 80	49.0	36.1	41.5	21.7	11.3	14.2
Chi-square	NS	0.004	0.003	0.001	0.0001	0.0001
			Cardiovascular mortality			
< 20	41.7	33.9	35.1	7.4	32.4	25.7
20-39	66.7	33.3	40.0	26.8	14.0	19.8
40-59	42.1	50.0	46.9	24.2	12.6	17.1
60-79	25.0	26.7	26.3	18.4	10.6	13.4
≥ 80	31.4	25.0	27.6	10.5	6.3	8.0
Chi-square	NS	NS	NS	0.0001	0.0001	0.0001

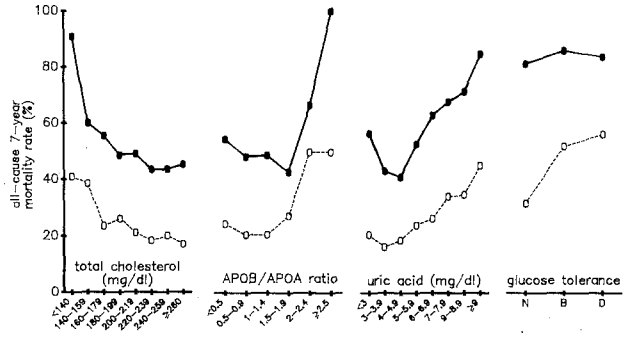

Figure 1. - All-cause 7-year mortlaity by total cholesterol, by the apolipoprotein B/apolipoprotein A ratio (APOB/APOA), by serum uric acid, and by glucose tolerance in the 318 very old subjects (*solid lines*) and in the 1910 subjects aged 65 to 79 years (*dashed lines*). N: normoglycemic, B: borerline, D: diabetic (see text for classification).

DISCUSSION

In the cohort of old people examined in this survey, arterial hypertension, which has a strong risk potential in young adults, was a very poor predictor of mortality; the 7-year mortality rate was not different between normotensive and hypertensive VOPs and OPs, and no clear trend of mortality in relation to blood pressure was detectable. Furthermore, in VOPs the highest mortality rate was found in the lowest blood pressure classes, i.e. < 130 mmHg systolic and 80 mmHg diastolic blood pressure.

These data are in agreement with those of Ekbom *et al.* (13) who demonstrated, in 961 elderly men and women aged ≥ 60 years, a very weak correlation between blood pressure and mortality. Similar data have been presented by Mattila *et al.* (21) (561 elderly subjects aged ≥ 85 years) and by Campbell *et al.* (4). Langer *et al.* (18) even described a "paradoxical survival" in elderly men aged 75 years or more having the highest blood pressure values. Finally, some authors found after antihypertensive treatment a higher mortality rate among subjects having lower diastolic blood pressure (< 85 or < 80 mmHg), although mortality remained high at the highest blood pressure values (J-shaped curve) (8, 9, 35).

By contrast, other authors have found a strong predictive value of arterial hypertension for excess cardiovascular disease in elderly subjects as well as in younger ones (1, 3, 16, 34) and have maintained the traditional premise of the lower the blood pressure, the better (20). Agner (1) found that hypertension had an independent predictive value for excess of cardiovascular 10-year mortality in women 70 years of age, and Kannel has stated that "*...some 30 to 60% of all cardiovascular disease in the elderly appears to be attributable to either mild or severe hypertension*" (19). However, the above mentioned studies did not include a great number of subjects aged 80 years or over.

Another strong and independent risk factor in young and middle-aged hypertensives is LVH (5). Mortality was higher in our VOPs having ECHO-LVH, while no relationship was found between ECG-LVH and mortality, in either VOPs or in OPs. LVDD, left atrial or aortic dimensions were not predictors of mortality among VOPs; only a weakly significant trend of mortality in relation to left atrium diameter was seen in OPs, but not in VOPs.

Other electrocardiographic abnormalities summarised in Table 5 (such as myocardial ischemia, RBBB or atrial fibrillation) were found more frequently in VOPs than in OPs. They were predictors of mortality in OPs, in agreement with data from other authors, who described a shorter life expectancy in middle-aged subjects having an abnormal electrocardiogram (23, 28). On the contrary, VOPs with or without ECG abnormalities had the same mortality rate, confirming that VOPs are different from younger age groups as regards prediction of mortality. Left atrial enlargement - independently of atrial fibrillation - was also insignificant among VOPs, while a statistically significant trend between mortality and left atrial dimension was detectable among OPs.

The analysis of data on blood lipids clearly shows that, in both VOPs and OPs, overall 7-year mortality did not increase, rather it tended to decrease in the highest quintiles of the cholesterol distribution curve. A similar trend, sometimes with a U-shaped curve, has recently been described by others in different age groups (2, 24, 31). In our survey this may not be attributed to a higher incidence of cancer in the lower cholesterol classes, as suggested by others (24, 30); in fact, cancer mortality was quite similar in the different cholesterol classes among both VOPs and OPs, and logistic regression demonstrated that cholesterol was not a predictor of cancer mortality in VOPs. Furthermore, both total cholesterol and triglyceride levels were higher in females, whose mortality was lower than that of males. As our survey included only elderly and very old persons, this trend without the second branch of the J-curve could also be due to a negative selection favouring, in the years before the survey, the survival of subjects having a better blood lipid pattern; in fact, total cholesterol, triglycerides and apolipoprotein B100 (Apo B) were quite low in our cohort. At variance with our observation, other authors found in non-population-based studies conducted in Scandinavian or North American subjects, a J-shaped relation between serum cholesterol and mortality (17, 30). As suggested by De Baker (10), Apo B levels could be a more precise predictor of mortality than total cholesterol. In our survey the ApoB/ApoA ratio showed a clear relationship with mortality, with an evident J-shaped curve and a dramatic increase in mortality rate above the value of 2.

In our experience, glucose intolerance and proteinuria were predictors of mortality only in OPs, but not in VOPs.

A very interesting relationship was found in both VOPs and OPs between blood levels of uric acid and mortality. The J-shaped curve for uric acid / mortality shown in Figure 1, with a dramatic increase above 6 mg/ml, cannot be interpreted by the fact that higher uric acid levels were correlated with either more advanced age or higher systolic blood pressure values (15, 25, 29), as both the systolic-adjusted and age-adjusted analyses show that mortality correlates with serum uric acid independently of these covariates. In 1989, Levine *et al.* described a strong and significant association between serum uric acid and overall mortality in the women of the cohort of the Chicago Heart Association Detection Project in Industry (19), where hypertensive subjects and those aged more than 64 years were excluded.

The reduction of FEV_1 was also a very good predictor of mortality in VOPs, at least in very old women, as well as in both women and men aged 65 to 79 years. Our data partially agree with those of authors who found impairment of lung function to be a risk factor in younger age groups (7, 29).

In conclusion, in our subjects 80 years of age and over some risk factors (hypertension, LVH, glucose intolerance, cholesterol, triglycerides and proteinuria), whose importance is definitely accepted in young adults, do not seem to predict mortality. On the contrary, other parameters (FEV_1, blood uric acid, ApoB/ApoA ratio) were critical in predicting mortality. Data on cardiovascular events other than mortality, derived from the longitudinal analysis of the *CASTEL*, are in order.

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