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Risk factors for cardiovascular disease in the very elderly: results of a cohort study in a city in southern Brazil

Maria Helena Werle[1], Emílio Moriguchi[2–4], Sandra Costa Fuchs[3], Neide Maria Bruscato[2], Waldemar de Carli[2] and Flávio Danni Fuchs[3,4]

Abstract

Background: Risk factors for cardiovascular mortality have barely been investigated in very elderly persons and there may be differences compared with younger individuals.

Methods: This is a cohort study of all inhabitants over 80 years of age in the city of Veranópolis, Brazil. The association of demographic, anthropometric, physical, and medical characteristics with mortality by any cause and by cardiovascular disease (CVD) was investigated by means of Cox regression models.

Results: The mean age of the participants was 83.6 ± 3.3 years. Vital status and cause of death was ascertained in 96.9% of the participants after a mean follow-up of 8.7 ± 3.8 years. Systolic and diastolic blood pressure showed a U-shape relationship with cardiovascular and total mortality. Blood pressure lower than 140/90 mmHg was associated with a higher risk for cardiovascular mortality (HR 4.76, 95% CI 1.56–14.28, $p = 0.006$). Duration of sleep was inversely associated with the risk of cardiovascular death (HR 0.83, 95% CI 0.73–0.95, $p = 0.007$), while apoA-I was inversely associated only with the risk of all-cause mortality (HR 0.99, 95% CI 0.98–1.00, $p = 0.041$). Anthropometric indexes, smoking, cholesterol, LDL-cholesterol, HDL-cholesterol, and other traditional risk factors were not associated with cardiovascular mortality.

Conclusion: Many traditional risk factors are not associated with cardiovascular mortality in the very elderly. Longer sleep duration is associated with lower cardiovascular mortality of very elderly individuals, while low blood pressure identifies very elderly individuals at higher risk of dying from cardiovascular causes.

Keywords

Very elderly, all-cause mortality, cardiovascular mortality, cardiovascular risk factors, blood pressure, hypertension, blood lipids, sleep duration

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Introduction

The rise in life expectancy has increased the proportion of very elderly people worldwide. Compared to younger elderly subjects, healthy very elderly individuals are at higher risk of presenting a first cardiovascular event and those who have had such an event are at an even higher risk of having a second one. Therefore, the identification of modifiable risk factors for the occurrence of cardiovascular outcomes in very elderly individuals should be pursued.

The power of classic risk factors to accurately predict risk of cardiovascular disease seems to diminish with advancing age.[1] Observational studies in the oldest individuals have shown that some of these risk factors become nebulous, or even act in the reverse direction, particularly in regard with their association with mortality by any cause. The association

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between blood pressure (BP) and total mortality is controversial.[2,3] Most studies have demonstrated higher mortality by any cause in people with the lowest BP[4–6] or a J- or U-shaped association between BP and mortality by any cause.[7–9] The association of cholesterol with total mortality in the very elderly is also controversial.[10] The association between other traditional cardiovascular risk factors with total mortality in the very old has been occasionally reported, but studies with cardiovascular outcomes are scarce.[11]

In Brazil, the life expectancy has steadily increased in the last few decades, and is nowadays reaching the duration observed in developed countries. A cohort of all inhabitants of Veranópolis over 80 years was launched in 1994 to investigate risk factors for cardiovascular disease.[12] In this report, we present the association between several risk factors for cardiovascular disease and the incidence of total mortality and mortality by cardiovascular causes after a mean follow-up of 8.7 ± 3.8 years.

Methods

Design

We used a prospectively planned cohort study.

Study population

The study population included all individuals over 80 years living in the city of Veranópolis in 1994. The population at the time of baseline evaluation was of 18,122 inhabitants, and 213 were over 80 years according to the population census done by the Brazilian Institute of Geography and Statistics. The population of Veranópolis has been stable and the rate of migration, particularly among the elderly, is almost nil.

Ethical aspects

The study was approved by the Ethics Committee of the São Lucas Hospital – Pontifical Catholic University of Rio Grande do Sul and by the Research Ethics Committee of the Federal University of Rio Grande do Sul. The participants or their relatives signed an informed consent to participate.

Measurement of baseline characteristics

All very elderly individuals were submitted to an extensive evaluation in the study clinic. Weight was measured with subjects minimally clothed without shoes, using digital scales and recorded to the nearest 100 g. Height was measured in a standing position, without shoes. BP was measured with a mercury sphygmomanometer (Erka, Germany) with a cuff appropriate for arm circumference, with the individuals sitting for at least 5 min before starting the measurements. Two measures were taken, keeping up intervals of approximately 30 min between. Hypertension was defined by systolic BP $\geq$ 140 mmHg or diastolic BP $\geq$ 90 mmHg and isolated systolic hypertension by systolic BP $\geq$ 160 mmHg and diastolic BP $<$ 90 mmHg. Prevalent baseline disease, such as cancer and cardiovascular disease, was specifically investigated by history, clinical examination, and laboratory examination when necessary.

Blood samples were collected after an overnight fasting (12 h or more) and the following blood tests were done: glucose, uric acid, total cholesterol, HDL-c, LDL-c, Lp (a), and triglycerides (TG). Total cholesterol, HDL-c, TG, and glucose were determined by enzymatic colorimetric methods using commercial kits and LDL-c was calculated according to the Friedewald equation for values of triglycerides below 400 mg/dl (samples with triglyceride values greater than 400 mg/dl were excluded). Diabetes was characterized by a prior medical diagnosis, use of medications for the treatment of diabetes, or blood glucose levels $\geq$ 126 mg/dl.

Physical activity was estimated by calculating the energy expenditure in kilocalories per week (kcal/week) during various activities, using the code of intensity proposed by Taylor et al.[13] In summary, all activities during a typical week, such as light and heavy housework, working in the yard, leisure activities, and exercise were recorded in hours per week. The number of hours spent on each activity was multiplied by an intensity code (kcal/min)[13] and the sum gave the energy expenditure per week. Total sleep time was measured by asking the subjects how much time they spent sleeping at night and napping during the day.

Alcohol intake was measured by the amount of alcohol ingested per week and was determined through the quantity-frequency method, based on the type of beverage consumed (in g/week) using standard measures of wine, beer, and distilled beverages and their alcohol content. Individuals were grouped into non-drinkers, moderate drinkers (men $\leq$ 210 g/week and women $\leq$ 105 g/week), and heavy drinkers (men $>$ 210 g/week and women $>$ 105 g/week). Individuals were classified as current smokers if they smoked at least one cigarette/day currently or stopped smoking less than two years previously.

Outcomes

The vital status of all participants was confirmed by home visits conducted between 2006 and 2009. The exact day of death was recorded. The cause of death was identified by death certificates and interviews with close family members, interviews of family physicians, specialists, and by checking the records of the city

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hospital just before the death. Two physicians, unaware of the baseline risks of the deceased participants, classified the causes of death into four groups in accordance with the WHO ICD-10: deaths by circulatory causes, malignancy, infections, trauma, and others causes. The deaths by cardiovascular causes included ICD-10 classified in the I-00 to I-99 codes.

Statistical analysis

Statistical analysis was performed using the SPSS version 16.0. Comparison of total and cardiovascular mortality by quartiles of continuous variables or categorical variables was done by the χ^2 test and tested for linear trend when appropriate. The association between the incidence of all cause and cardiovascular mortality by baseline selected risk factors was analyzed by means of Cox proportional hazards regression models, including time to event and adjusting for age (model 1) and by a full set of potential risk factors (model 2). Variables included in the model were those that showed at least a trend for association in the univariate analyses or that are well-known risk factors for total mortality or cardiovascular mortality. Deaths by other causes were censored in the models with cardiovascular deaths as outcome. Hazard ratios and their corresponding 95% confidence intervals were calculated. Models were run for the whole sample and excluded participants who reported cardiovascular disease or cancer at baseline, and participants who developed cancer during the follow-up.

Table 1. Selected baseline characteristics of the individuals (*n* and % or mean ± SD; $N = 187$)

Women	119 (63.6)
Smokers	12 (6.7)
Men	68 (36.4)
Age (years)	83.6 ± 3.3
Body mass index (kg/m^2)	26.7 ± 4.7
Waist–hip ratio	0.89 ± 0.07
Diastolic blood pressure (mmHg)	90.5 ± 12.8
Systolic blood pressure (mmHg)	168.1 ± 25.1
Hypertension (BP ≥ 140/90 mmHg)	174 (93)
Pulse pressure (mmHg)	77.5 ± 21.4
ApoA-I (mg/dl)	165.4 ± 33.7
ApoB-100 (mg/dl)	87.5 ± 21.0
Total cholesterol (mg/dl)	211.6 ± 47.4
LDL (mg/dl)	139.1 ± 42.5
HDL (mg/dl)	45.5 ± 12.6
Triglycerides (mg/dl)	137.2 ± 65.6
Blood glucose (mg/dl)	96.4 ± 27.3
Creatinine	0.86 ± 0.20
Diabetes mellitus[a]	32.0 (17.6)
Physical activity (Kcal/week)	5538.2 ± 4718.4
Total sleep (hours)	12.6 ± 3.1
Alcohol consumption (g/week)	208.3 ± 183.7
Years of schooling	2.3 ± 2.6

[a]Based on a diagnosis made by a physician, or blood glucose level ≥126, or use of medication for diabetes.

Results

There were 213 individuals of 80 years and over living in Veranópolis in 1996. In total, 193 (91%) were evaluated in the baseline. The vital status and cause of death was ascertained in 187 individuals (96.9%) of the original cohort between 2006 and 2009. The baseline characteristics of the participants are shown in Table 1. There was a higher number of women; the average BMI was within overweight limits and a large proportion had hypertension. The average number of drugs in use was 2.3 per participant. Just a few were current smokers and had diabetes, and most consumed alcohol (wine) and slept for long periods.

The relationship between the distribution of several characteristics, divided into quartiles or categories, and all-cause and cardiovascular mortality is shown in Table 2. Total mortality was directly associated with age and inversely with diastolic BP and ApoA-I. There was a trend for an inverse association between the number of hours of sleep and BMI and a trend for a direct association of diabetes mellitus with total mortality. The inverse relationship of BMI and total mortality was in part due to deaths by cancer ($p = 0.09$). The hazard ratios for cardiovascular mortality by quartiles or categories of risk factors (Table 2) were similar to all-cause mortality but most lost statistical significance. Total sleep persisted inversely associated with the risk of cardiovascular death, diastolic BP showed a trend for an inverse relationship, and LDL-cholesterol showed a trend for a non-linear relationship. BMI was inversely associated with total mortality but not with cardiovascular mortality, and waist–hip ratio was not associated with total and cardiovascular mortality. Education, gender, physical activity, alcohol consumption, smoking, and blood lipids (except ApoA-I) were not associated with total and cardiovascular mortality. Use of BP-lowering drugs in the baseline evaluation did not affect mortality from CHD or all-cause mortality.

Risks of cardiovascular death by selected cardiovascular risk factors, adjusting for age and for a full set of cardiovascular risk factors, are presented in Table 3.There was an inverse association of risk for cardiovascular death with total hours of sleep both in the models adjusted for age and for the full set of risk factors. BP below 140/90 mmHg had a strong and independent association with the risk of cardiovascular

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Table 2. Total mortality and cardiovascular mortality by distribution of baseline characteristics (quartiles or as otherwise stated)

	Deaths any cause			Cardiovascular deaths		
Characteristics	*N* (%)	*p* value	*p* for linear trend	*N* (%)	*p* value	*p* for linear trend
Age (years)[a]		.021	.002		.185	.173
1 (80-81)	28 (60.9)			9 (19.6)		
2 (81-83)	34 (72.3)			14 (29.8)		
3 (83-85)	38 (80.9)			19 (40.4)		
4 (86-94)	41 (87.2)			14 (29.8)		
Sex		.095			.904	
Women (*N*:119)	85 (71.4)			36 (30.3)		
Men (N:68)	56 (82.4)			20 (29.4)		
Years of Schooling[b]		.162	.911		.606	.498
0 (*N*: 49)	37 (75.5)			13 (26.5)		
1–3 (*N*: 92)	79 (85.9)			32 (34.8)		
> 4 (*N*: 25)	18 (72.0)			8 (32.0)		
Smoking		.173			.815	
No (*N*: 166)	123 (74.1)			50 (30.1)		
Yes (*N*:12)	11 (91.7)			4 (33.3)		
Alcohol consumption[c]		.750	.981		.323	.247
Abstemious (*N*:93)	69 (74,2)			23 (35,4)		
Moderate drinkers (*N*:44)	35 (79,5)			17 (50,0)		
Heavy drinkers (*N*:49)	36 (73,5)			16 (45,7)		
Physical activity (kcal/week)[a]		.193	.140		.447	.332
≤ 2357	33 (76.7)			10 (23.3)		
2358–4452	34 (77.3)			12 (27.3)		
4453–7329	35 (79.5)			17 (38.6)		
> 7330	27 (61.4)			13 (29.5)		
Total sleep (hours)[a]		.063	.037		.084	.012
1 (8-11)	34 (79.1)			16 (37.2)		
2 (11-12)	34 (79.1)			14 (32.6)		
3 (12-14)	34 (79.1)			11 (25.6)		
4 (14-23)	25 (73.8)			6 (14.0)		
Diastolic blood pressure (mmHg)[a]		.044	.055		.259	.076
≤ 81.7	41 (89.1)			19 (41.3)		
81.7 – 90.6	35 (74.5)			13 (27.7)		
90.6 – 99.0	30 (63.8)			13 (27.7)		
> 99.0	35 (74.5)			11 (23.4)		
Systolic blood pressure (mmHg)[a]		.373	.314		1.000	.949
≤ 150.7	39 (84.8)			14 (30.4)		
150.7–166.2	33 (70.2)			14 (29.8)		
166.3–187.3	34 (72.3)			14 (29.8)		
> 187.3	35 (74.5)			14 (29.8)		
Pulse pressure (mmHg)[a]		.515	.515		.950	.612
≤ 64.0	37 (80.4)			13 (28.3)		
64.0–78.0	32 (68.1)			13 (27.7)		
78.0–91.7	37 (78.7)			15 (31.9)		
> 91.7	35 (74.5)			15 (31.9)		

(continued)

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Table 2. Continued

	Deaths any cause			Cardiovascular deaths		
Characteristics	*N* (%)	*p* value	*p* for linear trend	*N* (%)	*p* value	*p* for linear trend
Body mass index (kg/m^2)[a]		.080	.012		.148	.357
≤ 22.9	40 (87.0)			15 (32.6)		
22.9–25.8	36 (76.6)			13 (27.7)		
25. –30.0	35 (74.5)			19 (40.4)		
> 30.0	30 (63.8)			9 (19.1)		
Waist–hip ratio[a]		.473	.940		.715	.764
≤ 0.84	37 (80.4)			16 (34.8)		
0.85–0.90	31 (67.4)			12 (26.1)		
0.91–0.95	35 (74.5)			12 (25.5)		
> 0.96	37 (78.7)			15 (31.9)		
ApoA-I (mg/dl)[a]		.004	.001		.268	.220
≤ 140.0	43 (93.5)			17 (37.0)		
141.0–160.0	33 (71.7)			12 (26.1)		
161.0–190.0	35 (74.5)			17 (36.2)		
>191.0	29 (61.7)			10 (21.3)		
ApoB-100 (mg/dl)[a]		.541	.205		.175	.351
≤71.0	39 (83.0)			17 (36.2)		
72.0–87.0	34 (73.9)			16 (34.8)		
88.0–100.0	33 (71.7)			8 (17.4)		
>101.0	33 (71.7)			15 (32.6)		
Glucose (mg/dl)[a]		.569	.482		.781	.623
≤83.0	38 (82.6)			15 (32.6)		
83.0–91.0	33 (70.2)			13 (27.7)		
92.0–102.0	35 (74.5)			16 (34.0)		
>103	35 (74.5)			12 (25.5)		
Diabetes mellitus		.077			.521	
Yes (*N*:150)	109 (72,7)			43 (28.7)		
No (*N*: 32)	28 (87,5)			11 (34.4)		
Total cholesterol (mg/dl)[a]		.676	.609		.374	.612
≤174.1	38 (80.9)			18 (38.3)		
174.1–209.9	33 (70.2)			11 (23.4)		
209.9–239.0	36 (76.6)			12 (25.5)		
>239.0	34 (73.9)			15 (32.6)		
LDL (mg/dl)[a]		.114	.407		.092	.559
≤108.9	40 (87.0)			19 (41.3)		
108.9–132.7	30 (65.2)			10 (21.7)		
132.7–167.0	35 (76.1)			10 (21.7)		
>167.0	34 (75.6)			16 (35.6)		
HDL (mg/dl)[a]		.114	.109		.941	.660
≤36.2	40 (87.0)			14 (30.4)		
36.2–43.3	35 (76.1)			15 (32.6)		
43.3–51.8	30 (65.2)			14 (30.4)		
>51.8	34 (75.6)			12 (26.7)		

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Table 2. Continued

	Deaths any cause			Cardiovascular deaths		
Characteristics	*N* (%)	*p* value	*p* for linear trend	*N* (%)	*p* value	*p* for linear trend
Triglycerides (mg/dl)[a]		.750	.850		.857	.549
≤95.4	37 (78.7)			15 (42.9)		
95.4–124.9	34 (73.9)			15 (46.9)		
124.9–153.6	33 (70.2)			12 (37.5)		
>153.6	36 (78.3)			13 (38.2)		

[a]Quartiles (in some analyses the participants do not add up to 187 due to missing values). [b]Arbitrarily defined in face of the low formal education of participants. [c]Moderate drinkers: intake of < 210 g/week for men and < 105 g/week for women; heavy drinkers: intake ≥ 210 g/week for men and ≥ 105 g/week for women.

Table 3. Hazard ratio for incidence of cardiovascular deaths in the presence of selected cardiovascular risk factors

	Cardiovascular deaths			
	Hazard ratio (95% CI)[a]	*p* value	Hazard ratio (95% CI)[b]	*p* value
Age (years)	.99 (0.92–1.08)	.897	.996 (0.91–1.01)	.938
Sex (M)	1.04 (0.59–1.84)	.886	1.18 (0.56–2.24)	.752
Total sleep (hours)	.86 (0.77–0.97)	.012	.83 (0.73–0.95)	.007
Current smokers[c]	.94 (0.34–2.70)	.938	.74 (0.19–2.91)	.672
Body mass index (kg/m^2)	.96 (.91–1.02)	.203	.96 (0.89–1.04)	.910
LDL cholesterol (mg/dl)	.99 (0.99–1.00)	.641	1.00 (0.992–1.009)	.910
HDL cholesterol (mg/dl)	.99 (0.97–1.07)	.581	1.01 (0.97–1.05)	.501
ApoA-I (mg/dl)	.99 (0.98–1.00)	.132	.99 (0.98–1.01)	.189
Glucose (mg/dl)	1.009 (1.001–1.018)	.034	.99 (0.98–1.02)	.818
Diabetes mellitus[c]	1.43 (0.73–2.80)	.294	1.14 (0.44–2.95)	.781
Blood pressure ≤ 140/90 mmHg)[c]	3.22 (1.36–7.96)	.008	4.76 (1.56–14.28)	.006

[a]Adjusted for age. [b]Adjusted for the full set of variables in the table. [c]Risk versus the individuals without the specified condition.

death. Blood glucose levels were associated only in the model adjusted for age. Isolated systolic hypertension was not associated with the risk of cardiovascular death after adjustment for the full set of confounders (HR 0.92, 95% CI 0.4–2.0, $p = 0.847$). Excluding participants with evidence of cardiovascular disease at baseline (43 individuals, 23.0%) did not substantially change the estimates or risks for cardiovascular mortality, but only total hours of sleep remained significantly associated (HR 0.82, 95% CI 0,68–0.98, $p = 0.034$) and BP below 140/90 mmHg persisted at the risk side but lost its formal significance (HR 3.84, 95% CI 0.44–33.3, $p = 0.225$). The diagnosis of heart failure at baseline was strongly associated with the risk of dying by cardiovascular disease (HR 2.89, 95% CI 1.35–6.19) in the multivariate analysis. The inclusion in the model of cardiovascular drugs in use at the baseline evaluation (yes/no) did not change the risk estimates substantially. Excluding participants with a previous diagnosis of cancer and those who developed cancer during the follow-up (45 participants, 24.1%) did not substantially change the risks for cardiovascular mortality.

In Cox regression models, ApoA-I and BP below 140/90 mmHg were inversely and independently associated with all cause mortality (Table 4). Isolated systolic hypertension was not associated with risk for all-cause mortality after adjustment for confounding (HR 0.99, 95% CI 0.64–1.54, $p = 0.970$).

Discussion

In this cohort study of almost all the very elderly individuals living in the city of Veranópolis, Brazil, it was possible to identify independent risk and protective factors for all-cause and cardiovascular mortality. Blood pressure below 140/90 mmHg emerged as an

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Table 4. Hazard ratio for total mortality in the presence of selected cardiovascular risk factors

	Deaths by any cause			
	Hazard ratio (95% CI)[a]	*p* value	Hazard ratio (95% CI)[b]	*p* value
Age (years)	1.02 (0.97–1.07)	.504	1.02 (0.96–1.08)	.489
Sex (M)	1.33 (0.94–1.88)	.111	1.33 (0.88–2.02)	.169
Total sleep (hours)	.95 (0.90–1.01).	.115	.95 (0.89–1.02)	.128
Current smokers	1.12 (0.6–2.07)	.732	.88 (0.41–1.89)	.745
Body mass index (kg/m^2)	.97 (0.94–1.10)	.154	.97 (0.93–1.02)	.224
LDL cholesterol (mg/dl)	.998 (0.994–0.003)	.460	1.001 (0.996–1.006)	.630
HDL cholesterol (mg/dL)	.99 (0.98–1.00)	.220	1.009 (0.99–1.03)	.477
ApoA-I (mg/dl)	.99 (0.988–0.998)	.007	.99 (0.98–1.00)	.041
Glucose (mg/dl)	1.01 (1.000–1.002)	.069	1.002 (0.991–1.012)	.782
Diabetes mellitus	1.38 (0.9–2.09)	.135	1.33 (0.7–2.40)	.251
Blood pressure $\leq$ 140/90 mmHg)	2.5 (1.37–4.54)	.003	4.0 (1.96–8.33)	<.001

[a]Adjusted for age. [b]Adjusted for the full set of variables in the table.

independent risk factor for total and cardiovascular mortality. Hours of sleep were inversely associated with the risk of cardiovascular and total deaths, while Apo-A-I was inversely associated with the risk of death by any cause. Other traditional risk factors, such as total cholesterol, HDL-cholesterol, LDL-cholesterol, diabetes, smoking, physical activity, education, and anthropometric measurements were not associated with total and cardiovascular mortality in this cohort of very elderly individuals.

Our findings are in accordance with the results of cohort studies that have identified an inverse relationship between BP and risk of death by any cause in people of 80 years and older.[4–6] Diastolic blood pressure had a U-shape association with the risk of cardiovascular death in our study. Very elderly individuals with BP lower than 140/90 mmHg had higher rates of cardiovascular mortality. The estimates were not substantially modified after exclusion of participants with cardiovascular disease in the baseline evaluation and of individuals with cancer or who developed cancer during the follow-up.

As far we know, no study has investigated the association of BP with cardiovascular disease exclusively in very elderly individuals. In the Collaborative Studies meta-analysis[14] of subgroups of very elderly individuals participating of cohort studies, systolic and diastolic BP were positively associated with the risk of death by coronary heart disease and stroke, but just a small proportion of the individuals were over 80 years of age.

The higher risk for cardiovascular events, particularly of coronary heart disease, is biologically plausible in individuals with low BP. With increasing age, there are generalized structural and functional changes in arterial circulation that contribute to alterations in regional blood flow and progression of atherogenesis and may lead to microvascular abnormalities.[15] High BP may be necessary to guarantee adequate cardiac and cerebral perfusion. Low BP could be also secondary to undiagnosed heart failure.[16] Nonetheless, the benefit to treating very elderly individuals with high systolic BP was established to prevent stroke and heart failure.[17] The prevention of total mortality was demonstrated in the HYVET trial[18] but was not confirmed in a recent meta-analysis.[17]

As expected, lower levels of ApoA-I were at the risk side for cardiovascular and total mortality in our cohort, reproducing the inverse association observed in studies with younger subjects.[19] The absence of association between HDL-C and cardiovascular mortality reflects its debatable risk in elderly individuals.[20]

Most studies have reported a U-shape association between hours of sleeping and cardiovascular events in the elderly.[21–24] In our cohort, the duration of sleep had a significant and independent protective association with all-cause and cardiovascular mortality, without any evidence for a U-shape relationship. As far we know, this is the first cohort study with very elderly individuals that explored this association controlled by a robust set of confounding characteristics. Longer periods of sleep may identify healthier very elderly individuals, but these findings need to be confirmed in other cohorts.

Our study has some limitations that deserve mention. Due to the low statistical power, we did include individuals with previous cardiovascular disease in the baseline evaluation in the main analysis, which may have enhanced the probability that risk factors for such condition became significant. The analysis without such individuals, however, generally confirmed the

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trends observed in the whole sample. Just a few individuals had BP below 140/90 mmHg at baseline, and could be at risk for higher cardiovascular mortality because of other reasons. The risk of dying, however, was independent of many confounders, and the analysis by quartiles of BP reproduced this trend for higher number of individuals at each category. A beta error may have occurred in the evaluation of risks associated with smoking habits and diabetes. The extensive evaluation of cardiovascular risk factors, including lipids, alcohol consumption, physical activity and others, together with a high rate of follow-up of the entire elderly population of a city, are strengths of our investigation.

In conclusion, blood pressure over 140/90 mmHg and longer sleeping hours are associated with lower cardiovascular mortality of very elderly individuals. Low blood pressure and high levels of ApoA-I are associated with lower total mortality in very elderly individuals. Low blood pressure may identify very elderly individuals at higher risk of cardiovascular mortality.

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Conflicts of interest

The authors do not have any conflicts of interest.

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