BLOOD PRESSURE 2001; 10: 205–211

Pulse Pressure: An Independent Predictor of Coronary and Stroke Mortality in Elderly Females from the General Population

ALBERTO MAZZA, ACHILLE C. PESSINA, PRIVATO GIANLUCA, VALÉRIE TIKHONOFF, ANDREA PAVEI AND EDOARDO CASIGLIA

From the Department of Clinical and Experimental Medicine, Laboratory of Epidemiology, University of Padova, Italy

Mazza A, Pessina AC, Gianluca P, Tikhonoff V, Pavei A, Casiglia E. *Pulse pressure: an independent predictor of coronary and stroke mortality in elderly females from the general population.* Blood Pressure 2001: 205–211.

The aim of this paper is to evaluate whether pulse pressure is an independent risk factor for coronary and stroke mortality in 3282 subjects (1281 males and 2001 females) aged ≥65 years, taking part in the CArdiovascular STudy in the Elderly (CASTEL). After dividing subjects into tertiles of pulse pressure, adjusted relative risk (RR) and confidence intervals (CI) for 14-year coronary and stroke mortality was evaluated for each tertile. Among females, coronary mortality rate was 2.7% in the first tertile of pulse pressure, 4.7% in the second (RR 1.38, 95% CI [1.15–2.66]) and 6.2% in the third (RR 2, CI [1.20–3.51]). Stroke mortality was 3.6%, 4.1% (RR 1.23, CI [1.02–2.23]) and 8.3% (RR 2.27, CI [1.37–3.74]), respectively. This trend was recognizable in normotensive, borderline and sustained hypertensive women, where mortality increased with rising pulse pressure. No relationship was found between pulse pressure and mortality in males. In elderly women, pulse pressure was a good predictor of coronary and stroke mortality, even superior to the label of hypertension. No matter how any given pulse pressure level was obtained, it was more predictive of both coronary and cerebrovascular mortality than belonging to a normo- or hypertensive category. *Key words: elderly, epidemiology, mortality, pulse pressure, relative risk.*

INTRODUCTION

Many epidemiological studies have established a different role of diastolic and systolic blood pressure on coronary and cerebrovascular risk [1–4]. It has also been suggested that diastolic blood pressure is more strongly related to cardiovascular risk below the age of 45 years and systolic blood pressure above this age [5, 6]. On the contrary, little has been done to investigate the role of the pulsatile component of blood pressure. The pulse pressure, defined as the difference between systolic and diastolic, is a good way to explore this component in clinical investigations.

The increase of pulse pressure is an age-related phenomenon [7] and the common belief is that it is an indicator of large artery stiffness [8]. The majority of studies evaluating the relationship between pulse pressure and cardiovascular disease was performed in middle-aged males [9–11], mainly hypertensive [12]. Only two studies [13, 14] investigated the role of pulse pressure in females from a general population, but age was ≤65 years in both.

The aim of the present study was to evaluate whether an increased pulse pressure could predict the risk of coronary and stroke mortality in men and women from a general population of elderly subjects.

PATIENTS AND METHODS

The CASTEL (CArdiovascular STudy in the ELderly) is a population-based prospective study enrolling 3282 subjects aged ≥65 years, representing 73% of elderly subjects from the Northern Italian towns of Castelfranco and Chioggia. The protocol of the study has been previously published elsewhere [15]. Briefly, at the initial screening, sphygmomanometric supine blood pressure and heart rate were measured in triplicate at 15-min intervals, and this procedure was repeated three times at 1-month intervals; the average of the last two of the nine measurements was taken into consideration both for the analysis of data and for calculating pulse pressure. Subjects having either a systolic blood pressure ≥ 160 mmHg, or a diastolic BP ≥ 95 mmHg, or having a history of hypertension, or taking antihypertensive drugs were considered as *sustained hypertensives*. Those with systolic values ranging between 140 and 159 mmHg and diastolic values between 90 and 94 mmHg without therapy were labelled as *borderline*. As 72% of men and 75% of women received antihypertensive medication, "antihypertensive therapy" as dichotomic covariate was included in the multivariate Cox analysis in order to adjust the results.

Historical data were recorded by means of a Rose's questionnaire [16]. Body mass index was calculated as the weight/squared height ratio. Subjects with frank diabetes (fasting blood glucose repeatedly >7 mmol/l or a history of diabetes or previous treatment with antidiabetic drugs)

Blood Press Downloaded from informahealthcare.com by Universitat de Girona on 11/03/14
For personal use only.

© 2001 Taylor & Francis on licence from Blood Pressure. *ISSN 0803-7051*

RIGHTSLINK

Table I. *General characteristics of population according to tertiles of pulse pressure*

	Males ($n = 1281$)			Females ($n = 2001$)		
	Pulse pressure ≤ 60 mmHg (1st tertile)	Pulse pressure 61–75 mmHg (2nd tertile)	Pulse pressure >75 mmHg (3rd tertile)	Pulse pressure ≤ 62 mmHg (1st tertile)	Pulse pressure 62–80 mmHg (2nd tertile)	Pulse pressure >80 mmHg (3rd tertile)
Age (years)	72.6 ± 5.0	72.9 ± 4.7	73.3 ± 4.8	73.4 ± 5.6	74.2 ± 5.3[a]	75.0 ± 5.4[ab]
Systolic blood pressure (mmHg)	136.6 ± 13.7	154.1 ± 12.4[a]	180.6 ± 19.1[ab]	139.0 ± 13.3	159.8 ± 12.3[a]	186.5 ± 19.8[ab]
Diastolic blood pressure (mmHg)	85.6 ± 10.9	86.9 ± 11.2	90.3 ± 11.4[ab]	86.3 ± 10.1	89.3 ± 10.7[a]	92.6 ± 12.7[ab]
Heart rate (beats/min)	73.3 ± 11.5	73.4 ± 11.4	74.8 ± 11.8	77.2 ± 10.9	77.5 ± 11.2	78.0 ± 11.5
Body mass index (kg/m^2)	25.3 ± 3.6	26.1 ± 4.0[a]	26.3 ± 3.6[a]	26.2 ± 4.6	27.0 ± 4.6	26.8 ± 4.5
Left ventricular mass index (g/m^2)	158.4 ± 38.6	184.7 ± 48.8	187.8 ± 50.4[b]	170.9 ± 42.1	179.4 ± 43.2	183.3 ± 52.4[a]
Serum cholesterol (mmol/l)	5.3 ± 1	5.3 ± 1	5.6 ± 1[ab]	5.8 ± 1.2	5.8 ± 1.1	5.9 ± 1.2
HDL-cholesterol (mmol/l)	1.4 ± 0.4	1.4 ± 0.4	1.4 ± 0.4	1.5 ± 0.4	1.6 ± 0.4	1.5 ± 0.4
Serum triglycerides (mmol/l)	1.3 ± 0.6	1.4 ± 0.8	1.4 ± 0.8[a]	1.4 ± 0.7	1.5 ± 0.7	1.6 ± 0.9[a]
Blood glucose (mmol/l)	5.7 ± 1.2	6.1 ± 1.4[a]	6.3 ± 1.5[a]	5.9 ± 1.8	6.1 ± 1.9	6.4 ± 2.2[a]
Diabetes (%)	8.9	14.5[a]	16.7[a]	13.9	18.6	22.9[a]
Serum uric acid (μmol/l)	327.1 ± 77.3	333.1 ± 77.3	339.0 ± 83.3	291.5 ± 83.3	303.3 ± 77.3	309.3 ± 77.3
Serum creatinine (μmol/l)	88.4 ± 17.7	88.4 ± 26.5	88.4 ± 26.5	79.6 ± 35.4	70.7 ± 26.5	70.7 ± 17.7

[a] $p < 0.01$ vs 1st tertile, [b] $p < 0.01$ vs 2nd tertile.

and those with pre-diabetic glucose intolerance (blood glucose between 6.1 and 7 mmol/l) were considered together as they showed a comparable survival in a previous analysis carried out in the same population [17]. In a randomly chosen subset of 504 subjects, left ventricular mass was calculated [18] from the following algorithm: $1.04 \times$ [(end-diastolic diameter + end-diastolic posterior wall thickness + end-diastolic septum thickness)^3—end-diastolic diameter^3]—13.6. Left ventricular mass index (in g/m^2) was calculated by dividing left ventricular mass by body surface area [19].

Mortality data

Mortality was monitored according to the Register Office and double-checked for causes of death by referring to hospitals, retirement homes or physicians' files. All records were coded jointly, according to ICD-9-CM. All death certificates and hospital charts were reviewed by a specially trained research physician supervised by another, more expert one, to accurately determine the cause of death. If necessary, a third physician was contacted to resolve any problem with uncertain data. No information about mortality was lost to follow-up. The codes were 410–414 for coronary artery disease (CAD) and 430–438 for cerebrovascular disease. Sudden death was not taken into consideration because its origin was uncertain in many cases. The analysis of coronary mortality was then repeated after excluding the 1008 subjects with clinical history of CAD.

Statistical analysis

Analysis of variance was used for comparing groups, and Pearson's χ^2 test to compare the prevalence of categorical variables. Pulse pressure as a continuous variable was divided into tertiles, and for each tertile the relative risk (RR) with 95% confidence intervals (CI) adjusted for confounders (age, body mass index, resting heart rate, cigarette smoking, alcohol consumption, serum total and HDL cholesterol, serum triglycerides, fasting blood glucose, proteinuria >200 mg/dl, history of angina pectoris, of myocardial infarction, of stroke or TIA, of intermittent claudication, of heart failure, and murmurs at the neck) was derived from multivariate Cox analysis [20].

After debate, the study was approved by the CASTEL Ethics committee. All subjects gave informed consent. The procedures followed were in accordance with institutional guidelines.

RESULTS

Mean age at entry was 73.6 ± 5.2 years (range 65–95 years), i.e. 73.1 ± 4.8 in the 1281 males and 74.2 ± 5.5 in the 2001 females ($p < 0.0001$).

Table II. *Results of the multivariate Cox equation for coronary and stroke mortality in women* (n = *2001*)

	χ^2 enter	χ^2 remove	Improvement χ^2	p value	RR (95% confidence intervals)
Coronary mortality					
Diabetes	23.3	15.9	21.3	<0.0001	1.60 (1.29–2.00)
Uric acid	18.4	7.7	11.7	<0.001	1.23 (1.17–1.74)
Historical CAD	17.0	5.5	6.8	<0.01	1.68 (1.09–2.60)
3rd tertile of pulse pressure	7.3	3.4	3.9	<0.005	1.80 (1.01–3.15)
Serum triglycerides	15.1	3.2	3.2	0.07 (NS)	–
Antihypertensive therapy	0.84	–	–	–	–
Serum cholesterol	1.45	–	–	–	–
Atrial fibrillation	1.2	–	–	–	–
Historical CHF	5.2	–	–	–	–
Historical stroke	3.6	–	–	–	–
Proteinuria	3.2	–	–	–	–
Murmurs at neck	0.02	–	–	–	–
LVH_{ECG}	0.7	–	–	–	–
Cerebrovascular mortality					
Historical stroke	23.3	11.3	19.6	<0.0002	5.21 (3.18–8.6)
3rd tertile of PP	7.2	3.9	5.5	<0.0002	2.27 (1.37–3.74)
Atrial fibrillation	14.1	7.8	10.3	<0.002	2.40 (1.42–4.01)
LVH_{ECG}	3.3	2.7	2.9	<0.03	1.72 (1.10–2.61)
Uric acid	6.1	2.3	5.7	<0.001	1.61 (1.04–2.61)
Diabetes	3.2	1.2	1.9	0.06 (NS)	–
Antihypertensive therapy	0.71	–	–	–	–
Historical CAD	3.74	–	–	–	–
Seum triglycerides	0.3	–	–	–	–
Serum cholesterol	0.7	–	–	–	–
Historical CHF	1.4	–	–	–	–
Proteinuria	0.2	–	–	–	–
Murmurs at neck	0.3	–	–	–	–

CAD, coronary artery disease; CHF, congestive heart failure; LVH_{ECG}, electrocardiographically detected left ventricular hypertrophy; NS, statistically insignificant.

In the three tertiles of pulse pressure, mean pulse pressure was 49.9 ± 8, 67.4 ± 4.6 and 90.6 ± 12.7 mmHg in males, and 52.7 ± 7.9, 70.8 ± 4.7 and 94.3 ± 13.3 mmHg in females, respectively (all tertiles: $p < 0.0001$ vs each other). Table I summarizes the general characteristics of the population according to gender and tertiles of pulse pressure. In both genders, systolic and diastolic blood pressure, left ventricular mass index, blood glucose and serum triglycerides progressively increased from the first to the third tertile of pulse pressure, while serum total cholesterol and body mass index progressively increased in males only.

At the 14th year, 1616 subjects were dead and 1666 censored (overall mortality rate 49.2%, 56% in males, 44.9% in females; $p < 0.0001$). In multivariate Cox analysis, pulse pressure appeared as an independent predictor of coronary and cerebrovascular mortality in females only (Table II), while in males it was always rejected from the Cox equation (data not shown). Inclusion of "antihypertensive treatment" as a covariate did not influence either coronary or cerebrovascular
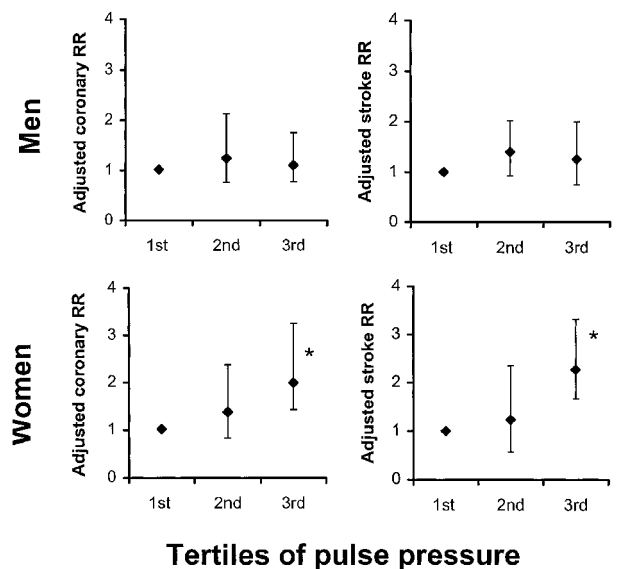

Fig. 1. Adjusted relative risk of coronary and stroke mortality among 3282 elderly subjects from general population, according to tertiles of pulse pressure.

Table III. *Number of coronary deaths by tertiles of pulse pressure (PP) in men and women*

	Men			Women		
	Blood pressure range in each tertile	All (*n* = 1281)	Without CAD (*n* = 945)	Blood pressure range in each tertile	All (*n* = 2001)	Without CAD (*n* = 1,329)
Tertiles of PP	PP range	14-year mortality		PP range	14-year mortality	
1st	≤60	19 (4.5%)	12 (3.4%)	≤62	18 (2.7%)	17 (2.6%)
2nd	61–74	22 (5.2%)	12 (3.5%)	63–79	31 (4.7%)	30 (4.6%)
3rd	≥75	20 (4.7%)	13 (3.9%)	≥80	41 (6.2%)[a]	37 (5.7%)[a]
All coronary deaths		61 (4.8%)	37 (3.9%)		90 (4.5%)	84 (6.3%)

The analysis was performed both including and excluding subjects who had clinically evident coronary artery disease (CAD) at the initial screening.
[a] $p < 0.005$ vs the 1st tertile.

mortality and was always rejected from the Cox equations of risk (Table II); this was also true, in particular, for diuretic therapy. Although diabetes was a strong predictor of coronary mortality (Table II), pulse pressure maintained its independent role after diabetes was included as a covariate in the multivariate Cox analysis.

Among females, 14-year coronary mortality rate was 2.7% in the first tertile of pulse pressure, 4.7% in the second (RR 1.38, CI [1.15–2.66]) and 6.2% in the third (RR 2.00, CI [1.20–3.51]). Stroke mortality was 3.6%, 4.1% (RR 1.23, CI [1.02–2.23]) and 8.3% (RR 2.27, CI [1.37–3.74]), respectively. No relationship was found between pulse pressure and the risk of coronary and stroke mortality in males (Fig. 1). After excluding from the analysis the women having CAD at the initial screening (Table III), a significantly higher coronary mortality was only observed in those who were in the third tertile of pulse pressure ($p < 0.005$ vs first tertile).

Table IV. *Fourteen-year coronary and stroke mortality rates*

Tertiles of pulse pressure (and range in mmHg)	14-year coronary mortality (%)	14-year cerebrovascular mortality (%)	Tertiles of pulse pressure (and range in mmHg)	14-year coronary mortality (%)	14-year cerebrovascular mortality (%)
*Normotensive subjects (*n = 451*)*					
Males (*n* = 209)			Females (*n* = 242)		
1st tertile (≤48)	1.4%	5.7%	1st tertile (≤49)	1.3%	1.1%
2st tertile (49–54)	1.4%	5.8%	2st tertile (49–55)	3.6%	3.8%
3rd tertile (>54)	5.7%	2.9%	3st tertile (>55)	6.3%	6.4%
$\chi^2 p$ value	NS	NS	$\chi^2 p$ value	<0.05	<0.05
All together	2.8%	4.8%	All together	3.7%	3.8%
*Borderline hypertensive subjects (*n = 1001*)*					
Males (*n* = 411)			Females (*n* = 590)		
1st tertile (≤60)	6.6%	2.2%	1st tertile (≤60	2.0%	4.1%
2st tertile (61–70)	5.1%	5.9%	2st tertile (61–70)	4.1%	4.6%
3rd tertile (>70)	5.8%	5.1%	3st tertile (>70)	7.1%	7.1%
$\chi^2 p$ value	NS	NS	$\chi^2 p$ value	<0.04	<0.05
All together	5.9%	4.4%	All together	4.3%	5.3%
*Sustained hypertensive subjects (*n = 1830*)*					
Males (*n* = 661)			Females (*n* = 1,169)		
1st tertile (≤70)	5.5%	5.0%	1st tertile (≤72)	3.9%	3.6%
2st tertile (71–87)	4.5%	6.8%	2st tertile (73–89)	4.1%	4.9%
3st tertile (>87)	4.1%	4.5%	3st tertile (>89)	6.3%	8.5%
$\chi^2 p$ value	NS	NS	$\chi^2 p$ value	<0.05	<0.01
All together	4.7%	5.5%	All together	4.7%	5.7%

A significant trend toward the increase of mortality with increasing pulse pressure is evident for females, not for males, in normotensive as well as in borderline and hypertensive subjects. Conversely, the differences between these three categories are insignificant.
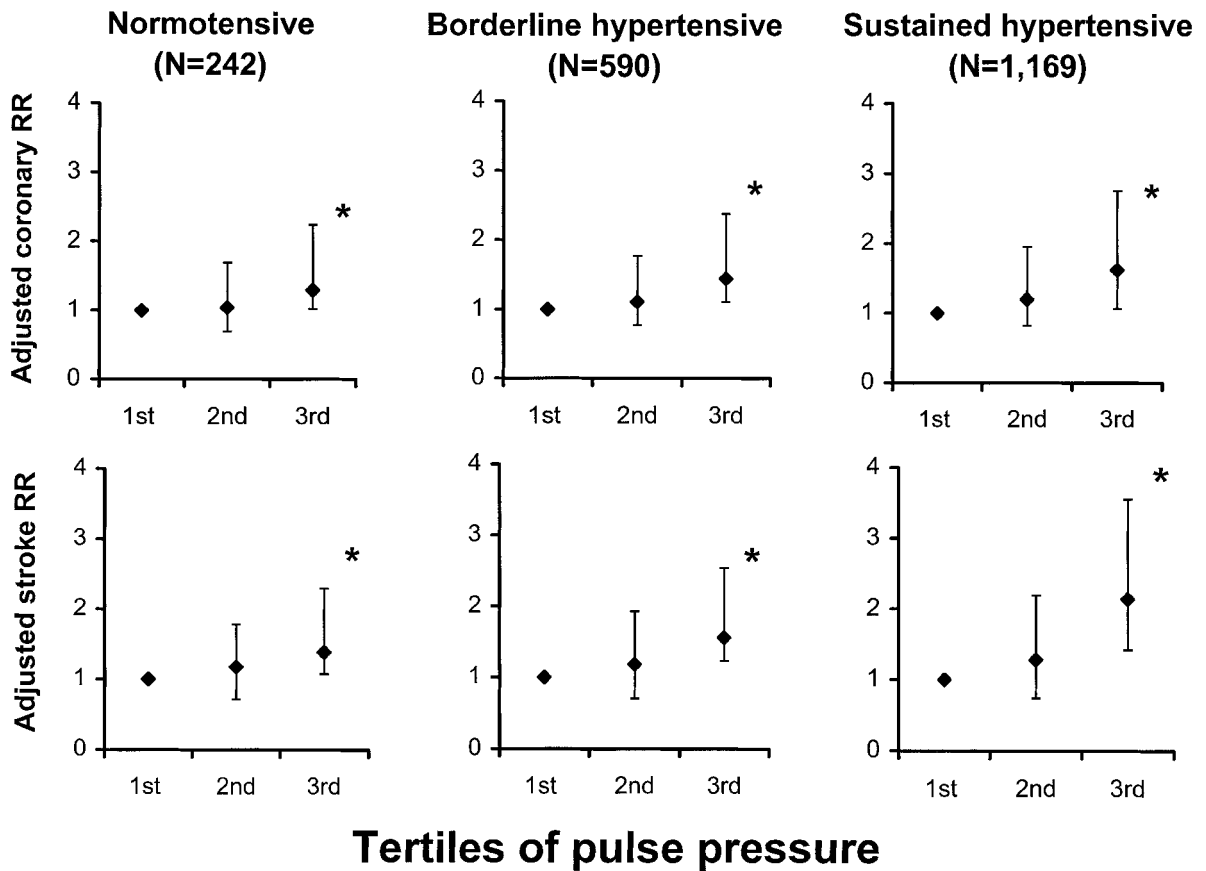
Fig. 2. Adjusted relative risk of coronary and stroke mortality among normotensive, borderline and sustained hypertensive elderly females from general population, according to tertiles of pulse pressure.

Finally, after dividing all subject into normotensive, borderline and hypertensive (Table IV), the above-mentioned trend of mortality in relation to pulse pressure was recognizable in borderline ($n = 590$) and in sustained hypertensive women only ($n = 1169$), as well as in the normotensive ones ($n = 242$). Adjusted relative risks are shown—separately for these three categories—in Fig. 2.

DISCUSSION

In the last two decades, there has been an increased interest concerning the prognostic role of pulse pressure in predicting cardiovascular disease. Several epidemiological studies have in fact demonstrated that office pulse pressure is a major predictor of cardiovascular risk in the general population [10, 13, 14], in subgroups of patients with essential hypertension [12], and also in survivors after acute myocardial infarction [21, 22]. Generally, males were studied in this respect, while few studies took women into consideration.

Moreover, the great majority of studies enrolled subjects below the age of 65 years (mainly around 45 years). Only one study considered elderly men [23], one elderly women [24], and yet another both genders together [25]. Scuteri *et al*. [23] demonstrated that pulse pressure accurately predicted cardiovascular events in females. Unfortunately, since the sample size was limited to 126 hypertensive women and the follow-up lasted 3 years only, the results—although of great interest—are difficult to extend to the general population. Furthermore, no comparison between males and females was provided in this study.

In the present study, which took into consideration elderly males and females recruited from the general population, pulse pressure was a good predictor of coronary and stroke mortality in women, but not in men (Fig. 1). This is in agreement with the finding that pulse pressure is the best blood pressure component for the prediction of carotid stenosis in women [26, 27].

In our study, pulse pressure was even superior to the label of "hypertension". In fact, mortality in the female's cohort increased with increasing pulse pressure, with no differences in this respect while passing from the "normotensive" to the "borderline" or "hypertensive"

category (Fig. 2). In other words, no matter how any given pulse pressure level was obtained, it appeared to be more predictive of both coronary and cerebrovascular mortality than belonging to normotensive or hypertensive category. High pulse pressure may derive both from rise of systolic (that is usual in the elderly) and from decrease of diastolic. In our population, the systolic component was prominent, as diastolic blood pressure remained unchanged or even increased a little with widening pulse pressure (in other words, systo-diastolic hypertension was more represented than isolated systolic hypertension).

Especially for elderly women, pulse pressure categorization may provide additional information than the usual categorization into normo- or hypertensive categories.

The question why pulse pressure is more strongly related to survival in females than in men is difficult to explain. It is not related to the greater prevalence of CAD in females than in males, since it was still present after exclusion of men and women having CAD at baseline. A potential explanation for the different impact of pulse pressure on mortality in males and females is that pulse pressure reflects arterial stiffness, which has a different natural history in men and women. In fact, arterial degenerative changes due to increasing age appear later in the women than in males [28, 29], and therefore stiffening does not occur until menopause [30]. Another possibility is that a natural selection have occurred in the previous decades in men who were most prone to succumb to high pulse pressure, subtracting them from our cohort and thus from observation [31].

Certainly, the demonstration of a strong predictive role of pulse pressure for mortality in women needs to be further researched and discussed, since results of several recent studies [23, 32] have shown a relationship between pulse pressure and cardiovascular mortality in males only. Nevertheless, these studies were not population-based, no comparison with females was provided and "cardiovascular mortality" was taken into consideration (so including not only coronary and cerebrovascular mortality, but also diseases of pulmonary circulation, hypertensive disease, chronic rheumatic heart consequences, diseases of arteries, arterioles, capillaries and veins, and other diseases of circulatory system).

In conclusion, our findings suggest that pulse pressure is an independent predictor of coronary and stroke mortality in elderly females. Therefore, determination of pulse pressure in the elderly may be of value in evaluating individual risk and possibly also therapeutic decision-making.

REFERENCES

1. Kannel WB, Dawber TR, McGee DL. Perspectives on systolic hypertension. The Framingham study. Circulation 1980; 61: 1179–82.
2. Hagman M, Wilhelmsen L, Wedel H, Pennert K. Risk factors for angina pectoris in a population study of Swedish men. J Chronic Dis 1987; 40: 265–75.
3. Tverdal A. Systolic and diastolic blood pressures as predictors of coronary heart disease in middle aged Norwegian men. Br Med J 1987; 294: 671–3.
4. Curb JD, Borhani NO, Entwisle G, et al. Isolated systolic hypertension in 14 communities. Am J Epidemiol 1985; 121: 362–70.
5. Ferguson JJ, Randall OS. Systolic, diastolic and combined hypertension. Differences between groups. Arch Int Med 1986; 146: 1090–3.
6. Kannel WB, Castelli WP, McNamara PM, McKee PA, Feinleib M. Role of blood pressure in the development of congestive heart failure. N Engl J Med 1972; 287: 781–7.
7. Safar ME. Editorial review—Pulse pressure in essential hypertension: a haemodynamic study. J Hypertens 1987; 5: 213–18.
8. Benetos A, Laurent S, Asmar RG, Lacolley P. Large artery stiffness in hypertension. J Hypertens 1997; 15: S89–97.
9. Kannel WB, Gordon T, Schawartz MJ. Systolic versus diastolic blood pressure and risk of coronary heart disease: The Framingham Heart Study. Am J Cardiol 1971; 27: 335–46.
10. Benetos A, Safar M, Rudnichi A, et al. Pulse pressure: a predictor of long-term cardiovascular mortality in a French male population. Hypertension 1997; 30: 1410–15.
11. Benetos A, Rudnichi A, Safar M, Guize L. Pulse pressure and cardiovascular mortality in normotensive and hypertensive subjects. Hypertension 1998; 32: 560–64.
12. Verdecchia P, Schillaci G, Borgioni C, Ciucci A, Pede S, Porcellati C. Ambulatory pulse pressure: a potent predictor of total cardiovascular risk in hypertension. Hypertension 1998; 32: 983–88.
13. Darne B, Girerd X, Safar M, Cambien F, Guize L. A pulsatile versus steady component of blood pressure: a cross-sectional analysis and a prospective analysis on cardiovascular mortality. Hypertension 1989; 13: 392–400.
14. Scuteri A, Cacciafesta AM, Di Bernardo MG, et al. Sex differences in correlates of steady state and pulsatile component of blood pressure. Clin Science 1996; 91: 385–389.
15. Casiglia E, Spolaore P, Mormino P, et al. The CASTEL project (CArdiovascular STudy in the ELderly): protocol, study design, and preliminary results of the initial survey. Cardiologia 1991; 36: 569–76.
16. Rose GA, Blackburn H. Cardiovascular survey methods. Geneva: WHO, 1968.
17. Casiglia E, Pauletto P, Mazza A, et al. Impaired glucose tolerance and its covariates among 2079 non-diabetic elderly subjects. 10-yr mortality and morbidity in the CASTEL. Acta Diabetol 1996; 33: 284–90.
18. Devereux RB. Evaluation of cardiac structure and function by echocardiography and other noninvasive techniques. In Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis, and management. New York: Raven Press, 1990.
19. Hammond IW, Devereux RB, Alderman MH, et al. The prevalence and correlates of echocardiographic left ventricular hypertrophy among patients with uncomplicated hypertension. J Am Coll Cardiol 1986; 7: 639–43.

20. Cox DR. Regression models and life tables. J Roy Statist Soc 1972; 34 Series B.

21. Madhavan S, Ooi WL, Cohen H, Alderman MH. Relation of pulse pressure and blood pressure reduction to the incidence of myocardial infarction. Hypertension 1994; 23: 395–401.

22. Mitchell GF, Moye LA, Braunwald E, *et al*. Sphygmo-manometrically determined pulse pressure is a powerful independent predictor of recurrent events after myocardial infarction in patients with impaired left ventricular function. SAVE investigators. Survival and Ventricular Enlargement. MA. Circulation 1997; 96: 4254–60.

23. Lee ML, Rosner BA, Weiss ST. Relationship of blood pressure to cardiovascular death: the effects of pulse pressure in the elderly. Ann Epidemiol 1999; 9: 101–107.

24. Scuteri A, Cacciafesta M, Di Bernardo MG, *et al*. Pulsatile versus steady-state component of blood pressure in elderly females: an independent risk factor for cardiovascular disease? J Hypertens 1995; 13: 185–191.

25. Franklin SS, Khan SA, Wong ND, Larson MG, Levy D. Is pulse pressure useful in predicting risk for coronary heart disease? The Framingham Heart Study. Circulation 1999; 100: 354–60.

26. Franklin SS, Sutton-Tyrrell K, Belle SH, Weber MA, Kuller LH. The importance of pulsatile components of hypertension in predicting carotid stenosis in older adults. J Hypertens 1997; 15: 1143–50.

27. Zureik M, Touboul PJ, Bonithon-Ko C, Courbon D, Berr C, Leroux C. Cross-sectional and 4-year longitudinal associations between brachial pulse pressure and common carotid intima-media thickness in a general population. The EVA Study. Stroke 1999; 30: 550–5.

28. Sonesson B, Hansen F, Stale H, Lanne T. Compliance and diameter in the human abdominal aorta: the influence of age and sex. Eur J Vasc Surg 1993; 7: 690–7.

29. Hickler RB. Aortic and large artery stiffness: current methodology and clinical correlations. Clin Cardiol 1990; 13: 317–22.

30. Jonason T, Henriksen E, Kangro T, Vessby B, Ringqvist I. Menopause is associated with the stiffness of the common carotid artery in 50-year-old women. Clin Physiol 1998; 18: 149–55.

31. Menotti A, Kromhout D, Nissinen A, *et al*. Short-term all-cause mortality and its determinants in elderly male population in Finland, the Netherlands, and Italy: the FINE Study. Finland, Italy, Netherlands Elderly Study. Prev Med 1996; 25: 319–26.

32. Benetos A, Zureik M, Morcet J, *et al*. A decrease in diastolic blood pressure combined with an increase in systolic blood pressure is associated with a higher cardiovascular mortality in men. J Am Coll Cardiol 2000; 35: 673–80.

Address for correspondence:

E. Casiglia, MD
Department of Clinical and Experimental Medicine
Via Giustiniani
IT-2-35128 Padova
Italy
Tel: 39-49-8212275 .
Fax: 39-49-8754179 .
E-mail: edoardo.casiglia@unipd.it