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Blood Pressure Trend and Cardiovascular Events in Nuns in a Secluded Order: a 30-Year Follow-up Study

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30-year data are presented on blood pressure and cardiovascular morbidity and mortality for 144 nuns living in a secluded order in six nunnerlie in Umbria, central Italy and 138 lay women from the same region. There were no significant differences at baseline regarding age, blood pressure, body mass index, race, ethnic background, menarche, family history of hypertension or 24-hour urinary sodium excretion. None of the women were smokers and none took birth control pills nor did they use estrogen replacement therapy. During the observation period blood pressure remained remarkably stable among the nuns. None showed a rise in diastolic blood pressure to above 90 mm Hg. On the contrary the lay women showed the expected rise in blood pressure with age. This resulted in a gradually greater difference ($\Delta >$ 30/15 mm Hg) in blood pressure between the two groups, which was statistically significant. There were 31 fatal and 69 non-fatal cardiovascular events during the 30 years of follow-up. These were significantly more common in the lay women, 10 vs. 21 fatal and 21 vs. 48 non-fatal in the nuns and lay women respectively. It appears reasonable to assume that the difference in psychosocial stress is the main underlying factor for the observed findings. *Key words: hypertension, psychosocial stress, ageing, cardiovsacular morbidity.*

INTRODUCTION

In industrialized societies blood pressure progressively increases with age [1–3], but the phenomenon is not an integral part of the ageing process. In fact, the age-related increase in blood pressure is not observed in primitive cultures where hypertension is virtually unknown, even though some exceptions in hunter-gathered populations are reported [4].

At present it is difficult to pinpoint the determinants of blood pressure differences in selected primitive and industrialized populations. In addition to the genetic factors, the increase in blood pressure with age is mainly focused on extrinsic factors such as diet, salt consumption, exercise, body weight and personal habits related to maladaption of humans "with atavistic homeostatic response to modern lifestyle and more mental rather than physical threats" [5].

Lifestyle influences on population blood pressure trend have been confirmed through longitudinal observations, even though possible mechanisms involved are difficult to identify and to standardize [6]. Preliminary findings point strongly toward the negative influence of high-stress areas with marked socio-economic problems on blood pressure levels [7, 8]. In contrast, a stress-free environment seems to reduce the increase of blood pressure over time [9, 10] and, consequently, the risk of cardiovascular events [11].

We have previously published the results of a longitudinal study aimed at determining the role of ageing in blood pressure changes in a group of white nuns in a secluded order, who showed no increase in arterial pressure over 20 years [12, 13].

In the present investigation, we analysed further correlates of arterial blood pressure in the same group of nuns and in a control group of lay women who were followed up for 30 years. Moreover, cardiovascular events were compared between the two groups.

METHODS

Study population

The primary objective of the present prospective longitudinal study was to extend our investigation into the role of ageing in blood pressure trends in a group of 144 nuns living in a secluded order in six nunneries in Umbria, central Italy.

The second objective was to investigate cardiovascular fatal and non-fatal events among nuns and control women during the study time.

The secluded nuns represent a human model of life

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differing in several aspects from the standard in industrialized and acculturated societies. The main difference is the daily living pattern, which alternates worship, prayer and physical work according to Saint Benedict's dictum "*ora et labora*" (pray and work). Their activities are performed in the peace of the convent, isolated from urban life and modelled on the monastic rule of almost absolute silence. They are physically and mentally alert with no anxiety for their future. They do not cope with economic and familiar stress, competition or social and political tensions. A group of 138 healthy, normotensive, ordinary women living in close proximity volunteered to undergo the clinical and laboratory procedure established in the protocol and were included as a control group. Women from both groups were consecutively recruited with no selection parameters.

The protocol used for the present study was approved by a local ethical committee for the protection of human beings and the participants gave their informed verbal consent.

Recruitment began in January 1964, finished in December 1968 and the follow-up continued for about 30 years.

Data collection

Details of our study population have been described elsewhere [12, 13]. In brief, this is an ongoing survey including a clinical evaluation, anthropometric and blood pressure measurements, humoral investigation and questionnaires.

All women were asked about their demographic data, personal medical history, educational levels and personal hygiene habits. Medical history was mainly focused on parental hypertension, later controlled by an objective ascertainment. Information about hygiene included current alcohol intake (g/week), smoking status, menstrual history, oral contraceptive used and dietary intake evaluation (detected by detailed diet interviews).

Anthropometric measurements, physical examinations and blood pressure determinations were performed every 6 months.

Height, measured in centimetres to the nearest 0.5 cm below, and weight, expressed in kilograms to the nearest 0.5 kg below, were used to compute body mass index (kg/m^2).

Blood pressure was measured in the right arm of a seated subject after a 10-min rest using a standard mercury sphygmomanometer; Korotkoff phases I and V were used to define systolic and diastolic blood pressure. Three consecutive readings were averaged for analysis. Over the premenopausal period, blood pressure was taken during the same phase of the menstrual cycle to avoid the well-known influence of sex hormones on blood pressure values [14]. About 90% of all blood pressure measurements were taken by one examiner.

Blood samples for cholesterol and triglyceride analyses were drawn into vacutainers and centrifugated within 1 h; serum was separated promptly and stored at +4°C.

A 24-h urine collection was made randomly for sodium measurement in a subset of 72 nuns and 67 control women. The storage period for serum and urine did not exceed 7 days. Total serum cholesterol and triglycerides were measured by a single laboratory according to methods reported elsewhere [15, 16]. Urinary sodium content was determined by flame photometry.

After initial evaluation all women underwent periodic clinical visits, blood pressure measurement, anthropometric examination and humoral investigation.

Criteria for cardiovascular outcome

Cardiovascular morbidity and mortality were expressed as the outcome of non-fatal and fatal events. Cardiovascular events included myocardial infarction, angina pectoris, severe congestive heart failure, coronary artery bypass surgery, sudden death, stroke, transient cerebral ischaemic attack and documented thrombotic occlusion of a retinal artery: myocardial infarction was diagnosed according to at least two of three standard criteria (typical chest pain, electrocardiogram QRS changes and transient elevation of the myocardial enzyme by more than twice the upper normal laboratory limits); angina pectoris was defined by reported chest pain accompanied by a typical ischaemic pattern on the electrocardiogram; stroke was diagnosed on the basis of the rapid onset of a localizing and persistent neurological deficit; transient ischaemic attack was defined by the diagnosis, made by a physician, of any sudden focal neurological deficit lasting less than 24 h; and sudden death was defined as a witnessed death that occurred within 1 h after the beginning of acute symptoms.

Statistical analysis

The significance of differences of categorical data between the two groups on entry was examined by one-way analysis of variance (ANOVA) and by non-parametric tests, as appropriate in the distribution of the variations considered. Multiple linear regression for continuous measures was assessed and comparisons between the two groups were estimated using the slope of the regression line (β coefficient) according to standard methods.

Repeated-measure ANOVA was also used to compare

Table I. *Biological and laboratory variables*[a] *at baseline examination*

Variable	Nuns ($n = 144$)	Control women ($n = 138$)
Age (years)	38.2 ± 5.7	34.7 ± 4.8
Age range (years)	22 – 58	25 – 46
Age at menarche (years)	14.3 ± 2.1	13.2 ± 2.7
Family hypertension (n =%)	27 – 18.7	22 – 15.9
Height (cm)	159.1 ± 6.3	161.7 ± 5.9
Weight (kg)	59.7 ± 3.4	58.3 ± 4.6
Body mass index (kg/m^2)	23.4 ± 0.3	22.3 ± 0.2
Supine blood pressure (mmHg)		
Systolic	125.6 ± 5.9	128.2 ± 7.4
Diastolic	79.1 ± 4.1	81.0 ± 4.4
Cholesterol (mg/dl)	201.1 ± 13	187.6 ± 17
Triglycerides (mg/dl)	135.4 ± 16	123.2 ± 22
Urinary Na^+ excretion (mEq/24 h)	144.3 ± 7.7	138.2 ± 9.9

[a] Vaues are means ± SD (except for age range and family history of hypertension).

the two groups over the 30-year period based on parametric values. Event rates were expressed as 1-year cumulative probabilities of cardiovascular events per 100 subjects, based on the ratio of the observed number of events to the total number of woman-years of exposure. For women who experienced two or more non-fatal events, the analysis included only the first event.

Survival curves were derived with the method of Kaplan and Meier [17]. Comparisons of curves were based on the log-rank test [18–20].

A two-sided probability of 0.05 or less was required for statistical significance. Numerical values are expressed as mean ± SD, unless stated otherwise.

RESULTS

Recruitment data

Table I presents the baseline demographic, anthropometric, clinical and laboratory data in the nuns and in the control women.

The nuns and the control women, all white, were similar in ethnic background, area of birth and familiar settlement. None of the study women changed their residence over the observation time. The nuns were generally less educated than the controls: 1.3% of the nuns were high-school graduates vs 3.6% of the control women; and 3.4% had learned a trade or qualified for teaching or a technical profession vs 13.8% of the lay women.

No significant difference was found in the family history of hypertension between the nuns (18.7%) and the controls (15.9%).

None of the women smoked or was taking birth control pills. A similar proportion of the nuns and control women reported low consumption of tea and coffee.

Mean weekly alcohol intake was 189 g in the nuns and 196 g in the controls (NS); two nuns and eight lay women did not use alcohol (NS).

Height, weight and body mass index were similar in the women of the two groups.

Mean systolic and diastolic blood pressure values for the entire baseline samples of the nuns were similar to those of the lay women.

No differences were observed in mean 24-h urinary sodium excretion between the groups. Serum total

Table II. *Selected follow-up of biological and laboratory variables for the two groups of women 6, 12, 18, 24 and 30 years after entry*

Variable[a]	Years				
	6th	12th	18th	24th	30th
Nuns					
Weight (kg)	60.1 ± 4.7	63.1 ± 5.0	64.3 ± 5.1	66.3 ± 5.3	69.4 ± 7.1
BMI (kg/m^2)	23.6 ± 0.3	25.0 ± 0.7	25.2 ± 0.5	26.1 ± 0.8	28.1 ± 1.0
Cholesterol (mg/dl)	222.1 ± 11.1	239.2 ± 12.4	242.1 ± 14.2	249.0 ± 16.3	254.0 ± 15.1
Triglycerides (mg/dl)	148.9 ± 16.2	159.2 ± 14.6	174.9 ± 16.1	181.6 ± 18.2	190.1 ± 17.1
UNA^+V (mEq/24 h)	138.2 ± 9.4	131.7 ± 8.2	133.6 ± 9.8	129.3 ± 2.9	141.3 ± 8.4
Lay women					
Weight (kg)	59.4 ± 5.9	61.5 ± 3.9	63.6 ± 5.1	66.6 ± 5.2	68.2 ± 8.6
BMI (kg/m^2)	22.9 ± 0.4	23.5 ± 0.5	24.3 ± 0.7	25.4 ± 0.9	28.4 ± 0.9
Cholesterol (mg/dl)	190.6 ± 16.3	228.1 ± 10.6	236.6 ± 17.1	241.1 ± 14.2	248.1 ± 16.1
Triglycerides (mg/dl)	143.3 ± 20.3	151.2 ± 13.8	155.1 ± 10.8	157.3 ± 17.2	170.4 ± 16.1
UNa^+V (mEq/24 h)	140.6 ± 8.4	132.2 ± 9.4	129.3 ± 10.4	131.3 ± 7.7	138.1 ± 7.7

[a] BMI = body mass index; UNa^+V = urinary sodium excretion.

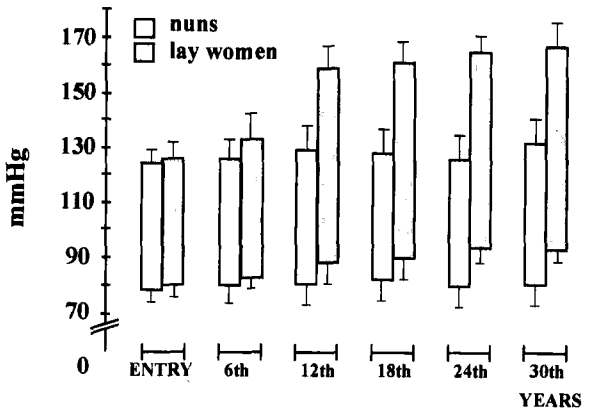

Fig. 1. Mean values (±SD) of systolic and diastolic blood pressure in the two groups at entry and every 6 years to the end of the follow-up.

cholesterol and triglycerides were higher in the nuns than in the control women ($p < 0.01$ for both).

Clinical follow-up

We obtained complete follow-up data from 282 of the 287 women who entered the study, from January 1964 to September 1996. The mean duration of the follow-up was 29.7 years (range 27.4–32.8). Increases in body weight and body mass index showed no difference between the two groups (Table II).

Age at menopause was similar between the nuns (45 ± 7 years) and the control women (47 ± 5 years).

None of the women used postmenopausal oestrogen compounds.

As expected, systolic and diastolic blood pressure values increased with age in the control women; in contrast, blood pressure remained virtually unchanged in the nuns over the 30-year period (Fig. 1). A highly significant difference in both systolic and diastolic blood pressure was detected between the two groups since the 12th year after entry ($p < 0.001$ for both).

Table III shows the regression equations of systolic and diastolic blood pressure values on age in the nuns and the control women by age subset at study entry (21–30; 31–40; 41–50 years).

The β slope of the systolic and diastolic blood pressure increase with age was significantly higher in the control women than in the nuns for each of the three age subsets ($p < 0.0001$ for all).

In the nuns the slope of both systolic and diastolic blood pressure generally approximated to zero level.

In relation to parity, systolic blood pressure increased with age significantly more in the lay women with at least one child than in the no-parity control women (β coefficient 1149 vs 1059; $p < 0.01$), while diastolic blood pressure was not affected by parity over time. However, both systolic and diastolic blood pressure increased over 30 years significantly more in the no-parity control women than in the nuns ($p < 0.001$ for all).

Mean values of total serum cholesterol and triglycerides in the 6th, 12th, 18th, 24th and 30th year after entry increased in parallel, even if the baseline differences between the two groups remained nearly unchanged over the follow-up period (Table II).

Random urinary sodium concentrations were similar in both cohorts at any follow-up examination (Table II).

Table III. *Regression equations of systolic and diastolic blood pressure (BP) on age in nuns and lay women by age subset at entry*

Variable	Age (years)	Intercept	β slope	SEM (β)	t value	p value	95% Confidence interval for β slope	
							Low	High
Systolic BP								
Nuns	21–30	127.29	0.068	0.0318	1.96	0.0734	−0.019	0.130
Controls		121.13	1.148	0.0204	59.28	0.0000	1.110	1.196
Nuns	31–40	127.88	0.072	0.0216	3.64	0.0027	0.020	0.108
Controls		126.52	1.046	0.0181	101.19	0.0000	1.039	1.084
Nuns	41–50	129.18	0.021	0.0192	1.33	0.2916	−0.016	0.068
Controls		134.92	0.992	0.0401	27.04	0.0000	0.910	1.084
Diastolic BP								
Nuns	21–30	79.68	0.0358	0.0201	1.77	0.0918	−0.005	0.075
Controls		77.92	0.4341	0.0089	52.58	0.0000	0.416	0.456
Nuns	31–40	78.04	0.0516	0.0130	4.06	0.0003	0.024	0.076
Controls		81.53	0.3666	0.0061	63.48	0.0000	0.344	0.374
Nuns	41–50	80.96	−0.0084	0.0141	0.56	0.5866	−0.033	0.019
Controls		82.68	0.3148	0.0156	21.61	0.0000	0.271	0.336

Cardiovascular events

We documented 100 cardiovascular events (31 fatal and 69 non-fatal). Among the fatal events there were 16 strokes, nine myocardial infarctions and six sudden deaths.

Figure 2 shows survival curves for fatal cardiovascular events. There were 10 events in the nuns and 21 events in the control women. Comparison between survival curves was slightly statistically significant ($p = 0.04$).

As for non-fatal events, there were 21 women with stroke, six with transitory ischaemic attack, eight with myocardial infarction, 13 with new-onset angina and ischaemic electrocardiographic pattern (two of whom underwent coronary revascularization), two with thrombotic occlusion of a retinal artery and 19 with new-onset congestive heart failure. There were 21 non-fatal events in the nuns (0.77 per 100 woman-years) and 48 events in the control women (1.66 per 100 woman-years). Comparison between survival curves (Fig. 3) was highly significant ($p \leq 0.0056$).

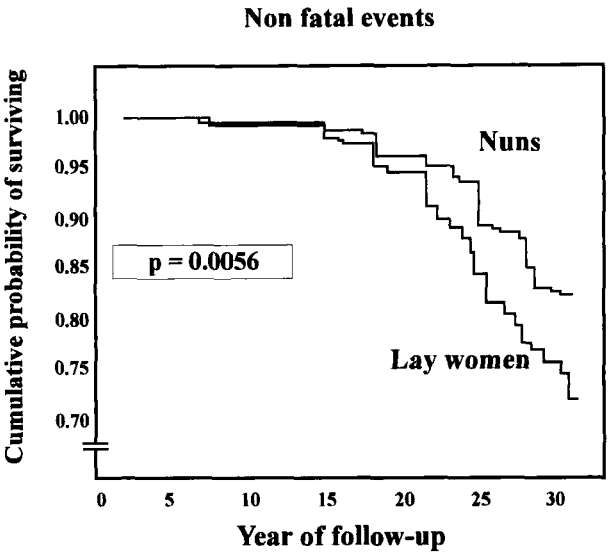

Fig. 3.

DISCUSSION

The present prospective study confirms and extends our previous results [12, 13] related to blood pressure trends in unselected nuns living for a long time in a secluded order. In consideration of the lack of blood pressure increase with age, persisting over 30 years, the question arises as to why the unusual phenomenon occurs in the nuns.

At baseline examination, nuns and control women were similar with respect to the main biological variables (age, race, ethnic background, age at menarche, parental and sibling history of hypertension, body mass index). Some selected lifestyle variables that might be correlated with differentiating blood pressure change with age can be excluded because of their absence in the two groups (tobacco, hormone contraceptives) or their equal distribution (use of alcohol, coffee, tea).

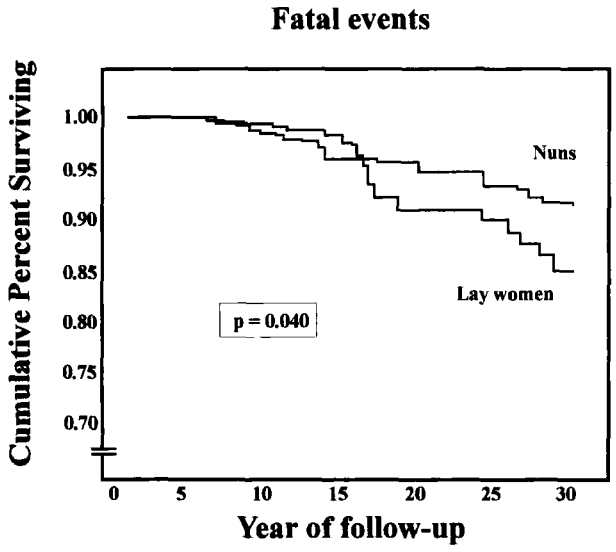

Fig. 2.

Menarche and menopause occurred at comparable ages in the two groups of women, even if there is no evidence that they might affect blood pressure change [21, 22]. Parity does not seem to have had a definite role in modulating the different blood pressure trends between nuns and lay women. Indeed, although systolic blood pressure alone increased with age more in the control women who had experienced childbirth than in those who had not, the mean slope of the regression line on both systolic and diastolic blood pressure in relation to age remained significantly higher in the no-childbirth lay women than in the nuns.

The control women were better educated, but the different educational level may not have affected the age-related blood pressure change, in accordance with the results of other studies [23–25]. On the other hand a subset of nuns ($n = 48$) and control women ($n = 53$) of comparable educational level at baseline maintained different blood pressure trends over 30 years.

The similar increase in weight and body mass index in the two cohorts over time suggests that the anthropometric pattern does not necessarily contribute to blood pressure change. This finding is consistent with the results of other studies [6, 26], showing that overweight and blood pressure increase may not be related.

Even salt intake did not influence the different blood pressure trend with age in the two groups, because 24-h urinary sodium excretion, although estimated in a random

sample from both groups, was similar between the nuns and control women. The association between sodium and blood pressure in observational studies is still a controversial topic [27–29]. Our data, in accordance with others [30, 31], do not support the role given to dietary sodium as a possible link between weight gain and blood pressure elevation [32].

Although serum cholesterol and triglycerides did not directly contribute to blood pressure change over time [33], they were higher in the nuns than in the control women, perhaps as a consequence of a generally lipid-rich diet in the convents.

Therefore, the main different variable in the two groups of women seems to be their way of life, even if the possible contribution of other dietary (i.e. calcium, potassium) or non-dietary variables in differentiating between the two groups was not investigated.

The relative role of psychosocial stress factors in respect of inducement and maintenance of blood pressure increase with age, both in animals and in humans, is a longstanding hypothesis not yet completely supported [34].

A variety of "emotional" response patterns can be elicited at the limbic–hypothalamic level by challenging environmental stimuli, and such a mechanism, if repeated over time, may contribute to blood pressure increase with age [35]. Some studies support the hypothesis that increased feeling of conflict and anxiety leads to hypertension over time [34, 36]. Anxiety, as measured by the Framingham Tension Scale, is regarded as the only psychosocial factor to predict blood pressure increase with age [23].

Conflict, anxiety, aggression and competition are virtually absent in the habitat of secluded nunneries, which present low psychological demands. Living for 30 years in such a low psychosocial stress environment appeared to prevent the increase of blood pressure with age.

Living in nunneries is associated with low cardiovascular morbidity. In fact, fatal and non-fatal events were exceedingly lower in the nuns than in the control women over a 30-year follow-up. The observed difference in mortality and morbidity rates between the two groups adds new questions to the evidence of the low cardiovascular risk in the nuns.

Low cardiovascular mortality and morbidity noted in the women in a secluded order resemble what may be observed in some traditional populations of the Melanesian Islands. According to a clinical cross-sectional study in Kitava, one of the Trobriand Islands of Papua New Guinea, Melanesia, where a subsistence lifestyle uninfluenced by western habits and psychosocial stresses is still maintained, stroke and ischaemic heart disease appear to be virtually absent in these inhabitants [11–37]. Of the analysed variables, leanness and low diastolic blood pressure seem to offer the best explanation for the unusual phenomenon in the Kitava population [11].

In our study, mean diastolic blood pressure appeared to be no greater than 90 mmHg in the nuns over a 30-year period.

On the other hand, the women of both groups had not had any beneficial effects, in the postmenopausal age, by oestrogen replacement therapy—notably associated with a favourable cardiovascular disease risk factor profile [38]—as none of them had used it.

Among the potential cardiovascular risk factors that might be implicated in differentiating cardiovascular event rates over 30 years between the two groups, tobacco as well as oral contraceptives can be excluded because, as mentioned above, their use was absent in the women of both groups.

Similarly, increase in weight and body mass index was equally distributed between the nuns and the control women.

Serum cholesterol and triglycerides seem not to be implicated in differentiating the cardiovascular event rate because, paradoxically, both lipid levels were higher in the nuns than in the lay women throughout the control period.

Physical activity, even though not measured, does not seem greater in the control women than in the nuns, because the latter perform daily many manual activities in the peace of the nunnery.

Our 30-year study adds to the evidence that hypertension and cardiovascular events are low in a human population with a preserved, peaceful, traditional lifestyle. The nuns offer a portrait of the real woman, largely free of hypertension, coronary risk and stroke, living today in a unique part of westernized society [39]. Their portraits resemble that of men relatively free of coronary heart disease living on the island of Crete [40]. Crete, Kitava island and the Umbrian nunneries provide a great opportunity to further explore the role of environmental factors in determining the diseases of civilization: hypertension, coronary heart disease and stroke.

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