Long-term Follow-up of Blood Pressure in Family Members of Soldiers Killed During the War in Bosnia and Herzegovina

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Aim To asses prevalence of essential arterial hypertension in family members of soldiers killed in 1992-1995 war in Bosnia and Herzegovina.

Methods The study enrolled 1144 subjects who lost a family member in the war and 582 of their close neighbors who experienced no such loss. Data on their medical history and habits were collected, and their blood pressure was recorded in 1996 and 2003. Arterial hypertension was defined as systolic blood pressure ≥140 mm Hg (≥130 mm Hg in patients with diabetes mellitus), or diastolic blood pressure ≥90 mm Hg (≥80 mm Hg in patients with diabetes mellitus), or taking antihypertensive therapy. Additional laboratory and clinical tests were performed in subjects with hypertension.

Results The prevalence of hypertension at both time points was higher in the group with a killed family member than in the group without the loss (55.1% vs 42.1%, $P<0.001$ in 1996, and 50.7% vs 39.0%, $P<0.001$ in 2003, respectively). However, there was also a significant decrease in the prevalence of hypertension in the group with the loss in 2003 ($P<0.001$), but not in group without the loss. Posttraumatic stress disorder (PTSD), smoking, and alcohol consumption were more prevalent in the group with a killed family member, but not cholesterol and triglyceride blood concentrations. In both groups, hypertension was more prevalent in subjects with PTSD and smoking or drinking habit. Proportion of subjects with hypertension who smoked and used alcohol was similar in both groups. Proportion of subjects with hypertension who did not smoke or drink was higher in the group with the loss (51.1% vs 36.7%, $P<0.001$; 46.2% vs 35.0%, $P = 0.006$; respectively).

Conclusion This study showed higher prevalence of hypertension in family members of killed soldiers, regardless of the presence of other cardiovascular risk factors. Only the stress of mourning was associated with higher prevalence of hypertension. Over time, proportion of hypertensive subjects with the loss decreased in the group with a killed family member, further suggesting that at least a part of their hypertension might have been of psychological origin.

Many studies investigated the effect of stress on various aspects of health status, but few found the association between stress and a particular disease (1-3). At the same time, the belief that stress causes and aggravates arterial hypertension is a widespread opinion among lay public, despite the lack of strong evidence. Arterial hypertension is currently defined as systolic blood pressure ≥140 mm Hg, or diastolic blood pressure ≥90 mm Hg, or taking antihypertensive therapy (4). In patients with diabetes mellitus, it is defined as systolic blood pressure ≥130 mm Hg, or diastolic blood pressure ≥80 mm Hg, or taking antihypertensive therapy (4). The exact etiology of essential arterial hypertension remains an enigma, primarily due to the high number of systems involved in the regulation of arterial pressure (5). Several factors are suggested as contributing to the hypertension – genetic factors, salt sensitivity, changes in ion homeostasis (sodium, potassium, and calcium), changes in renin-angiotensin-aldosteron system, insulin resistance, stimulation of sympathetic nervous system, and deficiency of vasodilator substances (5,6). Also, a number of environmental factors may have a role in the development of high blood pressure, such as salt intake, obesity, occupation, and alcohol intake (5). However, stress itself is not among them (5). This could be the consequence of the fact that it is very hard to design an objective study on the effect of stress on the arterial hypertension, due to substantial difficulties in defining, perception, and measurement of stress (7,8). A large study among employees of Australian government tax office showed no direct effect of job stress on blood pressure, but suggested a significant relationship of increased blood pressure and unhealthy habits, such as smoking, alcohol consumption, physical inactivity, and obesity, especially in men (9).

One of the most convincing, although unwanted, models of chronic stress is war. There are many studies on psychiatric health status of the soldiers and war veterans, dealing mainly with the evaluation of posttraumatic stress disorder (PTSD) (10-14), and a considerable number of studies investigating physical health of the soldiers (15-19). At the same time, somatic status of civilians affected by war was evaluated less frequently. A study on Afghan, Iranian, and Somali asylum seekers, and refugees living in the Netherlands showed that they suffered mainly from PTSD, depression, and anxiety (20), whereas the Israeli civilians had significantly higher levels of anxiety, despite the normal levels of cortisol and growth hormone (21). Several studies investigated the effect of the 1991-1995 war in Croatia. A study of prevalence of risk factors for cerebrovascular disease after the war in Croatia found significantly higher rate of arterial hypertension, hyperlipidemia, and obesity in people suffering from PTSD (22). A retrospective study on the prevalence of acute coronary syndrome before and during the 1992-1995 war in Bosnia and Herzegovina revealed increased number of acute myocardial infarctions and unstable angina pectoris cases during the war (23).

All of these studies evaluated the effects of general war stress on health, but none of them investigated the effect of the family member loss during the war, which is a frequent situation during military operations, and at the same time, an experience considered to cause great immediate stress reaction, as well as long-lasting psychological consequences (24) even in peace time. In this study, our aim was to investigate the prevalence of essential arterial hypertension in the family members of soldiers killed during the 1992-1995 war in Bosnia and Herzegovina, with the hypothesis that mourning may represent a stress that could affect arterial blood pressure.

Subjects and methods

Subjects

The study included 1726 subjects aged 18 and older from Western Herzegovina County, who

were the closest relatives (parents, grandparents, siblings, or spouses) of soldiers who fought in the 1991-1995 war in Bosnia and Herzegovina. The study group of subjects with a killed relative consisted of 268 families (1144 family members) of killed soldiers. Control group of subjects without a killed relative included 582 subjects (158 families) who lived in immediate neighborhood of families with a killed relative. The study group was significantly larger due to the fact that almost every family in this county had at least one family member joining the army, while many of them were killed. The two groups were similar in age and sex distribution and in the proportion of subjects who died between the two measurement points, 1996 and 2003 (Table 1). The enrolled families were, on average, five-member agriculture-oriented families.

Methods

In 1996, three physicians visited all the families included in the study and collected data on medical and psychiatric history of all family members, as well as their habits, such as smoking and consumption of alcohol and drugs. In addition, they performed the first measurement of arterial blood pressure, using mercury sphygmomanometer and auscultatory method as described elsewhere (25). If arterial hypertension was detected, the subject was advised to undergo basic laboratory blood tests, electrocardiography (ECG), and other clinical examinations recommended in the

evaluation of hypertension, such as fundoscopy and neurological examination (4). Arterial hypertension was defined as systolic blood pressure ≥140 mm Hg (≥130 mm Hg in patients with diabetes mellitus), or diastolic blood pressure ≥90 mm Hg (≥80 mm Hg in patients with diabetes mellitus), or taking antihypertensive therapy (4).

Laboratory tests, performed at the Široki Brijeg Health Center, Široki Brijeg, Bosnia and Herzegovina, included fasting blood glucose (normal plasma concentration: 3.6-5.6 mmol/L), creatinine (normal plasma concentration: 53-106 mmol/L), blood urea nitrogen (normal plasma concentration: 3.3-7.8 mmol/L), cholesterol (normal plasma concentration: 3.5-5.5 mmol/L, chlorenzimatic method), triglycerides (normal plasma concentration in men: 0.68-1.90 mmol/L; women: 0.46-1.60 mmol/L, chlorenzimatic method). Due to the financial reasons, laboratory tests and detailed physical examination were performed only in subjects with detected arterial hypertension, and the appropriate treatment was recommended afterwards.

During the study 112 subjects died, so the second measurement of the blood pressure performed in 2003 was done in 1072 subjects (93.5%) in the study group and 544 subjects (93.5%) in the control group.

Statistical analysis

Since variables showed deviation from normal distribution (Kolmogorov-Smirnov test), and

Table 1. Demographic characteristics of subjects enrolled in the long-term follow up of blood pressure in family members of soldiers killed during the war in Bosnia and Herzegovina*

Demographic data	No. (%) of family members		P†
	with a killed relative (n = 1144)	without a killed relative (n = 582)	
Age at the start of follow up (median, 25%-75% range)	50 (27.0-62.0)	52 (28.0-68.0)	0.591†
Sex:			
men	475 (41.5)	240 (41.2)	0.918‡
women	669 (58.5)	342 (58.8)	
Deceased during follow up	74 (6.5)	38 (6.5)	>0.950‡
Age of the deceased (median, 25-75% range):			
parents	64 (60-69) (n = 35)	57 (52-65) (n = 7)	0.100†
grandparents	77 (76-79) (n = 26)	75 (73-80) (n = 29)	0.382†

*The study involved 1726 closest relatives (parents, grandparents, siblings, or spouses) of the solders who fought in the war in Bosnia and Herzegovina during 1992-1995. Follow up lasted from 1996 to 2003.
†Mann-Whitney U test for age.
‡Fisher exact test.

there were significant differences in variances between studied groups (Leven's test for equality of variances), non-parametric tests were used. Differences in the prevalence between studied groups were tested by Fisher exact test. Exact McNemar test was used for testing the differences in prevalence between two time points. Mann-Whitney U test was used for testing the differences of measured variables between studied groups. All P values were two tailed and considered significant at <0.05, whereas Bonferroni correction was used for subgroup comparisons. Confidence intervals (CI) were estimated at the 95% level according to the recommended methods (26) and calculated by Confidence Interval Analysis 2.0.0 (CIA) statistical package (Trevor Bryant, University of Southampton, Southampton, UK). Analyses were performed by using SAS 8.02 software (SAS, Cary, NC, USA).

Results

In 1996, the prevalence of hypertension among subjects with a killed family member was 55.1% (Table 2), while the group without the loss had significantly lower proportion of hypertensive subjects (42.1%). In 2003, there were again more subjects with increased blood pressure in the study group (Table 2). However, when only the subjects still alive in 2003 were included in the analysis, the proportion of hypertensive subjects in the group with killed family member decreased from 53.1% in 2003 to 50.1% in 1996 (Table 3). At the same time, the prevalence of hypertension in the group without a killed relative did not change (Table 3).

Although all hypertensive subjects were advised to perform additional laboratory and clinical tests, not all of them reported back with the test results. The response rate was similar between the groups – 344 of 630 (54.6%) subjects with hypertension in the study group and 121 of 245 (49.4%) in the control group. Analysis of their clinical characteristics and habits in 1996 revealed no difference in the prevalence of diabetes, hypercholesterolemia, hypertriglyceridemia, or drug abuse between the two groups (Table 4). However, there was significantly higher prevalence of PTSD, smoking, and alcohol consumption among subjects with a killed relative (Table 4).

When we compared the prevalence of increased blood pressure between subjects who had PTSD, or a particular habit, we found significantly higher number of hypertensive subjects among people having PTSD or habit of smoking/drinking in the group with the loss, as well as in the group without the loss (Table 5). The results showed no group differences in the prevalence of hypertension among smoking subjects, as well as in the subjects who drink (Table 5).

Table 2. Prevalence of arterial hypertension at two follow up measurements of blood pressure in family members with and without relative killed during the war in Bosnia and Herzegovina*

Family member	No. of family members with arterial hypertension/total No. of subjects (%)†	
	1996	2003
With a killed relative	630/1144 (55.1)	543/1070 (50.7)
Without a killed relative	245/582 (42.1)	212/544 (39.0)
Group difference (%, 95% CI)‡	13.0 (8.0-17.8)	11.8 (6.7-16.8)

*The study involved 1726 closest relatives (parents, grandparents, siblings, or spouses) of the solders who fought in the war in Bosnia and Herzegovina during 1992-1995. Follow up lasted from 1996 to 2003.
†Arterial hypertension was defined as systolic blood pressure ≥140 mm Hg (≥130 mm Hg in patients with diabetes mellitus), or diastolic blood pressure ≥90 mm Hg (≥80 mm Hg in patients with diabetes mellitus), or taking antihypertensive therapy (4).
‡Fisher exact test, *P*<.001 for both 1996 and 2003; CI – confidence interval.

Table 3. Prevalence of arterial hypertension in 1996 and 2003 in the survived family members with and without relative killed during the war in Bosnia and Herzegovina*

Family members	No. (%) of family members with arterial hypertension		Group difference (%, 95% confidence interval)	*P‡*
	1996	2003		
With a killed relative (n = 1070)	568 (53.1)	543 (50.7)	2.3 (1.2-3.5)	<0.001
Without a killed relative (n = 544)	212 (39.0)	212 (39.0)	0 (-1.5-1.5)	>0.950

*The study involved 1144 closest relatives (parents, grandparents, siblings, or spouses) of the solders who were killed in the war in Bosnia and Herzegovina during 1992-1995. Follow up lasted from 1996 to 2003, during which time 74 persons died.
†Arterial hypertension was defined as systolic blood pressure ≥140 mm Hg (≥130 mm Hg in patients with diabetes mellitus), or diastolic blood pressure ≥90 mm Hg (≥80 mm Hg in patients with diabetes mellitus), or taking antihypertensive therapy (4).
‡McNemar's exact test, Bonferroni's correction.

Table 4. Clinical characteristics of subjects enrolled in a long-term follow up of blood pressure in family members of soldiers killed during the war in Bosnia and Herzegovina*

Disease/habit	No. (%) of family members		Group difference (%, 95% confidence interval)	P†
	with a killed relative (n = 1144)	without a killed relative (n = 582)		
Diabetes‡	45 (3.9)	14 (2.4)	1.5 (-0.3-3.1)	0.123
Increased cholesterol§, ‖	298 (86.6)	102 (84.3)	2.3 (-4.4-10.5)	0.543
Increased triglycerides¶, ‖	313 (91.0)	116 (95.9)	-4.9 (-9.1-0.9)	0.112
PTSD**	532 (46.5)	37 (6.4)	40.1 (36.5-43.5)	<0.001
Smoking††	563 (49.2)	233 (40.0)	9.2 (4.2-14.0)	<0.001
Alcohol††	646 (56.5)	242 (41.6)	14.9 (9.9-19.7)	<0.001
Drugs††	5 (0.4)	0	0.4 (-0.3-1.0)	0.174

*The study involved 1726 closest relatives (parents, grandparents, siblings, or spouses) of the solders who fought in the war in Bosnia and Herzegovina during 1992-1995. Follow up lasted from 1996 to 2003. All biochemical tests were performed in the laboratory of Health Center in Široki Brijeg, Bosnia and Herzegovina.
†Fisher exact test.
‡Self-reported; diagnosis of diabetes mellitus was established by a trained physician.
§Normal plasma concentration: 3.5-5.5 mmol/L (chlorenzimatic method).
‖Of all hypertensive subjects advised to perform laboratory tests, 344 (54.6%) responded in the study group, and 121 (49.9%) in the control group (P = 0.175, Fisher exact test).
¶Normal plasma concentration: 0.68-1.90 mmol/L for men; 0.46-1.60 mmol/L for women (chlorenzimatic method).
**PTSD – posttraumatic stress disorder, self-reported; diagnosis was established by a trained physician.
††Habit was considered to exist if self-reported, irrespective of the intensity.

Table 5. Association of arterial hypertension with posttraumatic stress disorder, smoking, and alcohol consumption in subjects enrolled in a long-term follow up of blood pressure in family members of soldiers killed during the war in Bosnia and Herzegovina (measured in 1996)*

Characteristic	No. of family members with hypertension and the habit†/ total No. of subjects with the habit (%)		Group difference (%, 95% CI)	P‡
	with a killed relative (n = 1144)	without a killed relative (n = 582)		
PTSD:				
yes	377/532 (70.9)	23/37 (62.2)	8.7 (-5.6-25.2)	>0.950
no	253/612 (41.3)	222/545 (40.7)	0.6 (-5.1-6.3)	>0.950
group difference (%, 95% CI)	29.5 (23.9-34.9)	21.4 (4.8-35.8)		
P‡	<0.001	0.09		
Smoking:§				
yes	333/563 (59.1)	117/233 (50.2)	8.9 (1.4-16.4)	0.138
no	297/581 (51.1)	128/349 (36.7)	14.4 (7.9-20.8)	<0.001
group difference (%, 95% CI)	8.0 (2.3-13.7)	13.5 (5.3-21.6)		
P‡	0.007	0.002		
Drinking:§				
yes	400/646 (61.9)	126/242 (52.1)	9.9 (2.6-17.1)	0.540
no	230/498 (46.2)	119/340 (35.0)	11.2 (4.4-17.7)	0.006
group difference (%, 95% CI)	15.7 (9.9-21.4)	17.1 (8.9-25.0)		
P‡	<0.001	<0.001		

*The study involved 1726 closest relatives (parents, grandparents, siblings, or spouses) of the solders who fought in the war in Bosnia and Herzegovina during 1992-1995. Follow up lasted from 1996 to 2003. PTSD – posttraumatic stress disorder; CI – confidence interval.
†Arterial hypertension was defined as systolic blood pressure ≥140 mm Hg (≥130 mm Hg in patients with diabetes mellitus), or diastolic blood pressure ≥90 mm Hg (≥80 mm Hg in patients with diabetes mellitus), or taking antihypertensive therapy (4).
‡Fisher exact test, Bonferroni's correction.
§Habit of smoking/alcohol drinking was considered to exist if self-reported, irrespective of the intensity.

There was significantly higher prevalence of hypertension among non-smoking and non-drinking subjects who lost a family member (Table 5). The two groups showed no difference in the prevalence of hypertensive subjects with PTSD as well as without PTSD (Table 5).

Discussion

The prevalence of essential hypertension in the family members of soldiers killed during the war in Bosnia and Herzegovina was higher than in the families without a killed relative. This was true for both measurement points, separated by a 7-year interval. In addition, while the prevalence of hypertension in the control group subjects still alive in 2003 did not differ in two time points, prevalence of arterial hypertension in the group with a killed family member decreased in 2003 compared with 1996.

Although this study was not designed to investigate a direct causative effect of the stress on the incidence of essential arterial hypertension, these results suggest association between family

member loss during the war and increased prevalence of hypertension. The two studied groups were similar in all other aspects except the loss of family member. If the constant prevalence of hypertension in the control group is understood as a consequence of general war stress, then the higher number of hypertensive subjects in group with a killed relative could be seen as a consequence of loss of the family member. This is in accordance with the findings of increased blood pressure and increased prevalence of hypertension, as well as increased number of acute coronary incidents, after general stress of terrorist or military operations (22,23,27,28). Our results would be more convincing if we had the real reference value of the blood pressure for each subject enrolled in the study, ie, if we had recorded blood pressure of all subjects before the war started, but obviously such an optimal follow up was impossible to perform due to unpredictability of the war.

Another interesting finding is a significant decrease of number of subjects with hypertension in the group with killed family member in 2003 compared with that in 1996, whereas the prevalence in control group did not change over time. Since the percentage of deceased subjects was similar in both groups, and since we included in the calculation for both time points only the subjects still alive in 2003, this decrease cannot be the consequence of different mortality rates in two compared groups. Although we would like to believe that decreased percentage of subjects with hypertension after 1996 is a direct effect of our intervention and treatment of (newly detected) subjects with hypertension, this is probably not the case, because we followed the same procedure in both groups and recommended evaluation and appropriate treatment of hypertension in both groups. Therefore, the obscured trend in this group with the loss could be an example of beneficial effect of time on the psychological trauma, according to old saying *"tempus omina vulnera sanat."*

Since factors other than stress can precipitate essential arterial hypertension (4-6), we compared laboratory findings and habits of subjects in two studied groups. The proportions of subjects with disturbed fasting blood glucose, cholesterol, and triglyceride concentrations were similar in two groups, indicating that the differences in hypertension were not due to these biological factors. However, there was a higher percentage of subjects suffering from PTSD and a higher rate of smoking and alcohol consumption in the group with killed family member. We then assessed whether higher prevalence of hypertension in the population with killed family member could be due to the higher prevalence of PTSD, smoking, and drinking in this group. The prevalence of subjects with hypertension who smoked or drank or had PTSD was strongly associated with the prevalence of arterial hypertension – irrespective of the loss of family member. These results are in accordance with the World Health Organization (WHO) and International Society of Hypertension (IHS) statement and other guides for arterial hypertension management (4-6), where smoking and drinking are pointed out as risk factors connected with arterial hypertension. However, they also show that higher prevalence of hypertension in the group with the loss was not due to the higher prevalence of PTSD, smoking, or alcohol consumption.

It is interesting that hypertension in non-smoking subjects with a killed family member was significantly higher than in the non-smoking subjects without killed family member. Also, there was higher proportion of non-drinking subjects with the loss having hypertension then among non-drinking subjects without the loss. Thus, if non-smoking/non-drinking subjects in both groups are considered free of other risk factors and differ only in the loss of family member in the war, this finding supports the notion that loss of a family member in the war is associated with increased blood pressure.

There are several debatable issues in this study. Study was aimed to investigate the prevalence of arterial hypertension in the family members of soldiers killed in the war. The presence of increased blood pressure is usually first detected by a general practitioner (GP). Since the standard mercury sphygmomanometer is usually in use in GP offices, we did not feel that sophisticated method for the blood pressure measurement, such as Hawkesley zero-muddling manometer, would be necessary for the simple detection of increased blood pressure. Furthermore, according to WHO and IHS statement on management of hypertension (4), the threshold for defining arterial hypertension in general population and in subjects with diabetes differ, so the nominal characterization of the presence and absence of arterial hypertension was more informative for our objective that exact values of blood pressure differences. Additionally, blood pressure in studied groups showed deviation from normal distribution and significant differences in variance between studied groups, probably due to large difference in the size of the groups, as the group of subjects with a killed relative was almost twice as large as the group of subjects without a killed relative; thus, parametric comparisons were not considered. Finally, although it is recommended that the control group should be at least equal in size or even twice as large as the study group, in this study we had the opposite situation. The study group was significantly larger (almost twice) due to the fact that in this county many men joined the army and many were killed, so the pool for recruiting families with family member who came back from the war was restricted.

In conclusion, our study showed that loosing a family member in the war possibly represented a stress that subsequently caused higher prevalence of arterial hypertension, irrespective of the presence of other cardiovascular risk factors, such as PTSD, smoking, alcohol consummation, diabetes, or hyperlipidemia. The prevalence of hypertensive subjects decreased over time, probably influenced by the beneficial effect of time on psychological basis of hypertension. Different study design that would exclude other stressful situations as is the war itself, should be applied to establish a direct causative relationship between death of the family member and incidence of essential arterial hypertension.

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