Pulzni tlak pri bolnikih z arterijsko hipertenzijo v Sloveniji

Pulse pressure in patients with arterial hypertension in Slovenia

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Izvleček

Namen: *Namen naše študije je bil določiti porazdelitev pulznega tlaka (PP), sistoličnega (SBP) in diastoličnega (DBP) krvnega tlaka v odvisnosti od spola in starosti ter ugotoviti odnos med PP, SBP in DBP. Analizirali smo podatke za 19972 bolnikov z arterijsko hipertenzijo v Sloveniji.*

Metode: *Podatke o meritvah arterijskega krvnega tlaka (SBP, DBP) na nadlahti smo pridobili pri več kot 360 družinskih zdravnikih iz zdravstvenih kartotek bolnikov. Večino podatkov smo zbrali v obdobju 2002–2006.*

Rezultati: *Povprečen PP je bil (71,2 ± 16,9) mmHg, povprečen SBP (172,8 ± 18,1) mmHg in povprečen DBP (101,6 ± 10,4) mmHg. Analiza z linearno regresijo je pokazala stati-*

Abstract

Purpose: *The aim of our study was to evaluate age– and gender–dependent pulse pressure (PP), systolic blood pressure (SBP), and diastolic blood pressure (DBP) distributions as well as their interconnected relationships in a large patient sample diagnosed with arterial hypertension in Slovenia.*

Methods: *Data on brachial arterial pressure measurements (SBP, DBP) were taken from the medical records of 19,972 arterial hypertension patients. More than 360 family medicine physicians participated in the study. The majority of the data was collected from 2002 to 2006.*

Results: *Mean PP, SBP and DBP were (71.2 ± 16.9) mmHg, (172.8*

stično značilno povezavo PP tako s starostjo (p < 0,001) kot tudi s spolom (p < 0,001). Pulzni tlak je naraščal s starostjo, pri moških in ženskah podobno. Ženske so imele statistično značilno višji PP (p < 0,001) kot moški v starostnem obdobju 35–65 let, razlika pa je bila manj izrazita po 80. letu starosti. Pulzni tlak je v črki U podobnem odnosu z DBP ter v skoraj linearnem odnosu s SBP.

Zaključek: *Rezultati naše študije kažejo, da je PP pri slovenskih bolnikih z arterijsko hipertenzijo odvisen tako od spola kot od starosti bolnika, na osnovi česar želimo spomniti na pomen upoštevanja PP pri načrtovanju antihipertenzivnega zdravljenja.*

± 18.1) mmHg and (101.6 ± 10.4) mmHg, respectively. Linear regression analysis showed a significant association of PP with age (p < 0.001) and with gender (p < 0.001). Pulse pressure increased similarly with age for men and women. Women had significantly higher PP than men during ages of 35 to 65 years (p < 0.001), but the difference was less evident for those above 80 years. Pulse pressure had a U–shape–like relationship with DBP, and a strong, almost linear relationship with SBP.

Conclusion: *The results of our study show age– and gender–dependent differences in PP distribution for Slovene patients with arterial hypertension. These findings may remind family medicine physicians to take PP values into consideration when planning antihypertensive therapy.*

INTRODUCTION

Pulse pressure (PP) is the difference between systolic (SBP) and diastolic blood pressure (DBP) values. With the loss of aortic compliance SBP increases with age, while DBP usually declines after age 60, leading to increased PP (1). Increased PP is an independent marker for cardiovascular (CV) disease risk, mainly for myocardial infarction, congestive heart failure, and CV deaths (2). The latest Slovenian Guidelines for the Management of Arterial Hypertension 2007 emphasized PP as a predictor of CV disease risk in the elderly (3). Few studies have previously investigated the therapeutic outcomes of targeting PP rather than mean blood pressure. Their focus was on finding differences among various anti–hypertensive groups of patients (4). Furthermore, PP is not only age– but also gender–dependent. Gender differences in age–dependent SBP and DBP distributions have been consistently observed in various populations, while the differences in PP distribution have been far less investigated (5).

To our knowledge, there has been no extensive study of PP distribution in the Slovenian population that focuses on age– and gender–dependent differences. Therefore, the first aim of our study was to evaluate age– and gender–dependent PP, SBP and DBP distributions in a large sample of patients with arterial hypertension in Slovenia. The second aim was to investigate inter–relationships between PP and SBP, or DBP in the same population.

MATERIAL AND METHODS

The study was cross–sectional and was conducted as part of the "Quality of Healthcare in Slovenia" project, in agreement with The National Medical Ethics Committee of the Republic of Slovenia (6). The majority of data was gathered during the five year period between 2002 and 2006 by more than 360 family medicine physicians. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

Collaborating physicians of family medicine collected data from the first 50 to 100 consecutive patients with arterial hypertension. Data on brachial arterial pressure (SBP, DBP) measured at the beginning of treatment, the age, and the patients' gender were taken from their medical records. All measurements were performed in a sitting position by physicians of family medicine, who were adequately qualified to measure

blood pressure and had the necessary equipment. Introductory lectures were prepared for instructing physicians, where it was clearly explained that only patients who had recorded blood pressure measurements before anti–hypertensive treatment should be included in the study. To minimize inclusion of extreme values we used the mean of three blood pressure measurements.

Patients under age 18, patients with missing values for any of the selected types of data (age, gender, SBP, DBP), and patients with normal arterial blood pressure (SBP < 140 mmHg and DBP < 90 mmHg) were excluded. The final sample included 19,972 patients with arterial hypertension.

Statistical analyses were performed using the Statistical Package for Social Sciences v18 for Windows (SPSS Inc.). Results are expressed as mean ± standard deviation for numerical variables and as frequencies for categorical variables. Linear regression analysis, with PP as a dependent variable, and age and gender as independent variables was performed. Due to the large sample size, $p < 0.001$ was considered statistically significant.

RESULTS

Study sample characteristics

Characteristics of the study sample are presented in Table 1. Among the 19,972 patients included in the analysis, there were 8444 (42.3%) men and 11,528 (57.7%) women; their mean age was (64.1 ± 12.1) years. Mean PP was (71.2 ± 16.9) mmHg, mean SBP was (172.8 ± 18.1) mmHg and mean DBP was (101.6 ± 10.4) mmHg. The distributions of PP, SBP, DBP values, and age of the patients according to gender, are presented in Table 2.

Pulse pressure distribution according to age and gender

Linear regression analysis showed a significant association of PP with age ($p < 0.001$) as well as with gender ($p < 0.001$). Pulse pressure in women increased constantly with age across almost all age groups, while PP increase in men was delayed. Women had significantly higher PP compared to men in ages 35 to 65 years ($p < 0.001$), but the difference was less evident for those above 80 years. Men had higher PP than women only before approximately 30 years. After age 60, men had a steeper increase in PP with age than women did. The biggest deviations of PP between men and women were before age 30 and during middle age.

Systolic blood pressure in both women and men showed an almost linear increase with age, while DBP in men showed a peak around age 45 and a decline thereafter. A peak DBP value for women was not well–defined and declined more gently with age compared to men (Figure 1).

Table 1: *Characteristics of the study sample*

	Minimum value	Maximum value	Mean value	Standard Deviation
PP (mmHg)	20	155	71.2	16.9
SBP (mmHg)	110	295	172.8	18.2
DBP (mmHg)	50	150	101.6	10.4
Age (years)	18.8	100.4	64.1	12.1

Abbreviations: PP–pulse pressure, SBP–systolic blood pressure, DBP–diastolic blood pressure

Table 2: *Characteristics of the study sample according to gender*

	Gender	Mean value	Standard Deviation	p
PP (mmHg)	men	68.7	16.9	<0.001
	women	73.0	16.7	
SBP (mmHg)	men	171.1	18.0	<0.001
	women	174.1	18.2	
DBP (mmHg)	men	102.4	10.5	<0.001
	women	101.1	10.2	
Age (years)	men	61.5	11.9	<0.001
	women	66.0	11.8	

Abbreviations: PP–pulse pressure, SBP–systolic blood pressure, DBP–diastolic blood pressure, p–probability

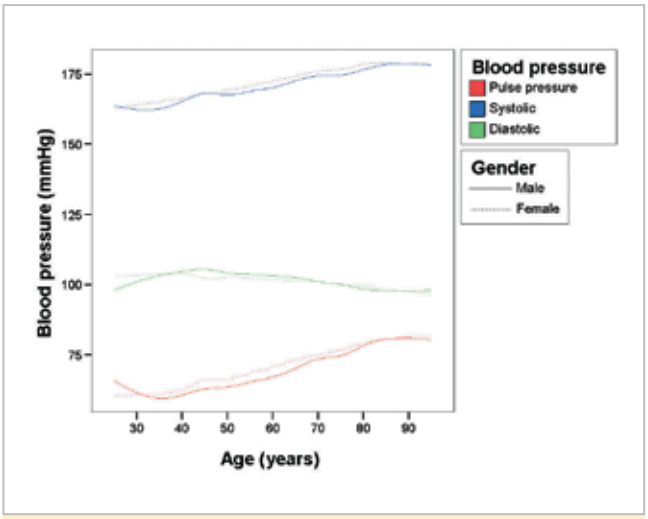

Figure 1. *Blood pressure distributions according to the age and gender of patients with arterial hypertension in Slovenia*
Abbreviations: PP–pulse pressure, SBP–systolic blood pressure, DBP–diastolic blood pressure

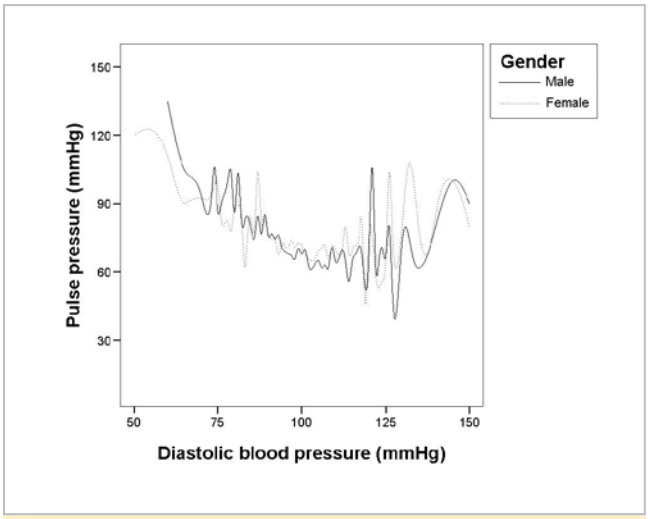

Figure 2. *Relationship between diastolic blood pressure and pulse pressure in patients with arterial hypertension in Slovenia*

Interrelationships of pulse pressure with diastolic and systolic blood pressure

Pulse pressure had a U–shape–like relationship with DBP (Figure 2), and in strong, almost linear relationship with SBP (Figure 3). The relationship between PP and SBP was similar for men and women. On the other hand, the differences in relationship between PP and DBP showed an apparent gender–bias.

DISCUSSION

In the present study we investigated age– and gender–dependent PP, SBP and DBP distributions as well as their inter–relationships in a large patient sample diagnosed with arterial hypertension in Slovenia. To our knowledge, this is the largest epidemiological study of PP in Slovenia.

The reasons for investigating PP distribution in the present study were as follows. Pulse pressure has been accepted as an independent predictor for CV disease risk. The prognostic role of PP is particularly important in high–risk and diseased populations (1). In patients with newly diagnosed hypertension and in patients with left ventricular dysfunction after myocardial infarction, elevated PP is a major risk factor for myocardial infarction and death (1). In the Framingham Heart Study, neither SBP nor DBP added to the predictive value of PP for coronary heart disease (7). According to the MRC Mild Hypertension Trial, PP was proposed to be a strong risk factor for coronary events in untreated hypertensive male subjects (8). The results of a follow–up study of the Multiple Risk Factor Intervention Trial (MRFIT) showed that, in older people, low DBP and high PP served as markers not only for higher CV disease risk, but also for possible end–organ damage related to greater CV disease risk. Considering the whole group of patients, SBP and DBP levels were more strongly related to CV disease when compared to PP (9). Another consideration is that PP distribution was found to be age– and gender–dependent in previous studies and may also differ among various populations (5). In addition, lowering PP may deserve special consideration during pharmacological treatment of arterial hypertension (4, 10).
Mechanisms involved in pulse pressure regulation are determined from both vascular and cardiac factors: the left ventricular ejection pattern, vascular compliance, as well as the timing and intensity of arterial wave reflections. Increased arterial stiffness

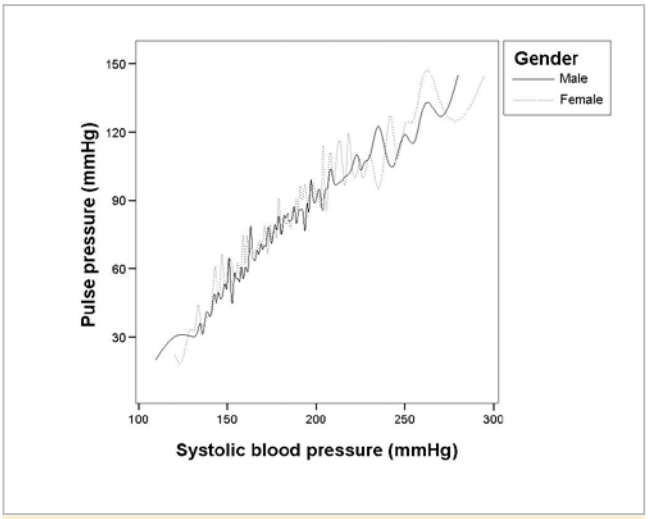

Figure 3. *Relationship between systolic blood pressure and pulse pressure in patients with arterial hypertension in Slovenia*

(stemming from central arteries) and alteration of wave reflections (generated at large and small arteries) or combination of both contribute independently to the increase in PP with age and hypertension. Another determining factor of PP is the cross–sectional architecture of the vascular system. In young subjects with arterial hypertension, alterations in the vessels' mechanical properties result mainly from the elevated pressure itself, while in the elderly, reduced compliance and distensibility are independent of blood pressure level (4, 11).

In our study, the mean PP for Slovene hypertensive patients was 71.2 mmHg ± 16.9 mmHg and the mean age was 64.1 years ± 12.1 years. In a similar study of 907 Slovene patients with arterial hypertension (mean age 62.3 years ± 11.9 years), the mean PP was 66.8 mmHg (12). Furthermore, in a study of 3067 Slovene people from the general population of ≥ 20 years (mean 65.2 years ± 12.1 years); the mean PP was 66.5 mmHg (13). The reasons for the high mean PP value in our study might be due to the following: (i) older patients, (ii) blood pressure measurements in patients with poorly controlled arterial hypertension, and (iii) no anti–hypertensive treatment for the majority of patients. Also, the mean PP for our patients was higher compared to a reference clinical value for the French population (50 mmHg) (14). According to various studies, a PP value higher than 60 mmHg is an independent predictor for CV disease risk (8).

An interesting observation in our study was that women had significantly higher PP, SBP and lower DBP compared to men from age 40 to 80 (mean SBP in women was higher, and mean DBP in women was lower than in men). After age 80, the difference in PP and DBP between men and women became less evident compared to middle–age patients. The results are contradictory to the results of a 12–year study on the blood pressure dynamics in Ljubljana adults, in which women had lower mean SBP and mean DBP than men (15). In a similar study on a non–selected French population containing 61,724 individuals, the PP value was higher in men than in women for the < 45 years age group, but for the > 45 years age group, the difference between men and women was reduced (14). In our population, women obviously had higher PP than men at a much younger age. However, it should be noted that women were significantly older than men and that all our patients were hypertonic. Gender differences exist for blood pressure regulation, which tends to change with age and are also cross–cultural. Arterial aging most likely stems from sex–related differences (5). In general, regardless of acculturation, women tend to have lower SBP during early adulthood but this variable rapidly increases with age, and results in a steeper climb of PP in women than in men. Pulse pressure may differ between men and women due to anthropometric factors, such as a relation between central pressure augmentation and height. Indeed, the augmentation index is greater in women compared to men; however, women have a somewhat faster heart rate (5, 16). There were also 15.4% more women than men included in our study. Age–dependent differences in PP trajectories between women and men most likely stem from gender–related differences in arterial aging and are consistent across different societies (5).

High PP was determined to be an independent CV disease risk factor, especially in the elderly (1). In our

study, PP increased with age (from approximately 40 years to 80 years) in a similar manner for both women and men. The increase in PP with age is physiological and cross–cultural. In older people, ventricular ejection is normal or even decreased and the main determinants of PP in such conditions are increased arterial stiffness and altered wave reflections (14). A study comparing PP distribution among unacculturated and partially acculturated non–selected populations showed similar results to ours, although the increase in PP in our study is steeper and the women in our study had higher PP than men (5).

In our study, PP had a strong, almost linear correlation with SBP and in a slightly stretched U–shape–like relationship with DBP. On average, the lowest PP occurred in patients with DBP ranging from 100 to 125 mmHg. This is partly in agreement with the results from another study on PP in older hypertonic patients, in which the lowest PP occurred at the highest DBP (1).

Our study is a cross–sectional survey, which may provide results that differ from longitudinal follow–up studies. The study sample is not representative for the general Slovene population since we included only patients with arterial hypertension. The PP value in our study had a higher baseline compared to other studies, and it is critical when interpreting the results. Blood pressure values were taken from medical records and measurements might vary among physicians.
It remains unclear whether increased PP should be treated independently of mean blood pressure. Evidence from randomized studies with morbidity and mortality end points are needed to determine the relative value of these therapies and whether the reduction of PP should be a specific treatment target. There is also increasing evidence that PP, unlike SBP and DBP, is minimally responsive to placebo, which is important for therapy as well as research. Pharmacotherapy for lowering PP should be oriented towards influencing arterial compliance, which include angiotensin–converting enzyme inhibitors and nitrates in addition to a low–salt diet. Other ways to lower PP are by decreasing ventricular ejection and change in arterial wave reflections (1).

CONCLUSION

The results from our study provide an overall insight in PP distribution for patients with arterial hypertension in Slovenia, which may have implications for treatment and disease prognosis. The main conclusions are: (i) PP increases with age for men and women; (ii) women had a significantly lower DBP, a higher SBP, and a progressively higher PP than men during most of the middle–age period; (iii) PP was almost linearly correlated with SBP and was in a stretched U–shape–like correlation with DBP. Our findings may have further useful implications in treating as well as in disease prognosis.

In the future, it would be interesting to study PP distribution in the general Slovene population and to review therapeutic differences of drugs proscribed for PP treatment, especially in the elderly.

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