ARTYKUŁ ORYGINALNY / ORIGINAL ARTICLE

24 hour ambulatory blood pressure values corresponding to office blood pressure value of 130/80 mm Hg

Ivan Rihacek¹, Petr Frana¹, Martin Plachy¹, Bohuslav Kianicka¹, Miroslav Soucek¹, Anna Vasku²

Abstract

Background: 24 hour ambulatory blood pressure monitoring (ABPM) values for patients who have office BP of 130/80 mm Hg have not been clearly reported.

Aim: The determination of ABPM values in treated hypertensive subjects corresponding to a mean office BP of 130/80 mm Hg.

Methods: BP measurement in subjects 40–70 years old, by ABPM and mercury sphygmomanometer. The inclusion criteria were: mean office BP systolic (SBP) 128–132 mm Hg and diastolic (DBP) 78–82 mm Hg. Seventy six subjects met all study inclusion criteria.

Results: Mean office BP: SBP 129.5 \pm 1.1 mm Hg, DBP 79.9 \pm 1.3 mm Hg. Mean 24 hour BP: SBP 121.9 \pm 2.0 mm Hg, DBP 73.1 \pm 1.9 mm Hg. Mean awake BP: SBP 124.9 \pm 2.4 mm Hg, DBP 75.5 \pm 2.2 mm Hg. Mean asleep BP: SBP 109.1 \pm 3.9 mm Hg, DBP 63.3 \pm 4.0 mm Hg.

Conclusions: The target values of ABPM identified in this study can be used in clinical practice and will contribute to risk stratification and treatment of hypertension.

Key words: population study, blood pressure measurement, office blood pressure 130/80 mm Hg, ambulatory blood pressure monitoring, corresponding blood pressure

Kardiol Pol 2013; 71, 7: 675-680

INTRODUCTION

With its high prevalence, hypertension is one of the major risk factors for cardiovascular disease (CVD). Target values of blood pressure (BP) are set arbitrarily on the basis of the results of large clinical trials. When measuring BP with a sphygmomanometer in a medical clinic (office BP), a value above 140/90 mm Hg is currently considered to be hypertensive [1, 2]. For some high-risk patients (diabetes patients with microalbuminuria/proteinuria and sub-clinical organ damage, post-stroke patients, and patients with nephropathy), the aim is to achieve a BP value of 130–139/80–85 mm Hg and possibly close to lower values in this range [3]. It has been shown that 24 hour ambulatory BP monitoring (ABPM) has a better predictive value of CVD risk than office measurements and allows the acquisition of more information about the tested individual (mean 24 hour BP, day and night BP, BP variability and diurnal rhythm of BP values)

[4, 5]. ABPM and home BP measurement are increasingly used in clinical practice and the results are no longer available only to specialised cardiologists. They are reviewed also by general practitioners; therefore, the criteria for evaluating the results of ABPM must be clear and simple. Also the new NICE clinical guideline 127 recommendation states that if the office BP is 140/90 mm Hg or higher, ABPM should by a confirmation of a diagnosis of hypertension [6].

The basic and most widely used BP measurement parameters are mean 24 hour, mean awake and mean asleep. Currently, the office BP value of 140/90 mm Hg corresponds to mean 24 hour ABPM value of 130/80 mm Hg, mean awake ABPM value of 135/85 mm Hg and mean asleep ABPM value of 120/70 mm Hg [1, 2]. Austrian authors have determined the average values of ABPM corresponding to different levels of hypertension classification during measurement of office BP by

Address for correspondence:

Ivan Rihacek, MD, PhD, 2nd Internal Department, University Hospital St. Anna, Pekarska 53, 65691 Brno, Czech Republic, tel: +420543182236, fax: 5431822312, e-mail: ivan.rihacek@fnusa.cz

Received: 17.07.2012 **Accepted:** 05.12.2012 Copyright © Polskie Towarzystwo Kardiologiczne

¹2nd Internal Department, University Hospital St. Anna and Masaryk University, Brno, Czech Republic

²Department of Pathological Physiology, Masaryk University, Brno, Czech Republic

sphygmomanometer according to the European Society of Hypertension (ESH) [7]. Corresponding office BP values to ABPM values are: office 135/85 mm Hg to ABPM 130/78 mm Hg, office 160/100 mm Hg to ABPM 140/88 mm Hg and office 180/110 mm Hg to ABPM 148/94 mm Hg. ABPM values that correspond to a target value of 130/80 mm Hg for BP during office measurement are not clearly defined. Relevant data is only to be found in a 2011 consensus position statement of ABPM in Australia [8], where office BP 130/80 mm Hg corresponds to ABPM 125/76 mm Hg.

The objectives of our study were: (1) to determine the mean values of ABPM (24 hour, awake and asleep) for hypertensive individuals 40–70 years old corresponding to an office BP of 128–132 and 78–82 mm Hg; (2) to calculate the mean arterial pressure (MAP) and pulse pressure (PP); and (3) to establish the 5^{th} – 95^{th} percentiles for the ABPM values of these groups of individuals.

METHODS Population studies

In our specialist hypertension clinic, the results of ABPM in hypertensive individuals examined in 1993-2011 were searched for male and female subjects 40-70 years old. 100% of the searched subjects were of Caucasian race. In all, 918 entries met these criteria and 832 valuable ABPM results were acquired. From these figures, individuals were selected who met the following inclusion criterion: office BP (measured by sphygmomanometer; the average of two measurements 1 min apart, at rest, with standard size cuff, and after 5 min in a sitting position) before ABPM was in the range 128–132 systolic (SBP) and 78–82 mm Hg diastolic (DBP). All ABPMs had hourly averages with a record during falling asleep and waking up. The mean of three measurements during the first ABPM had to be in the range 125-135 mm Hg SBP and 75-85 mm Hg DBP. Data where there was evidence of white-coat syndrome (mean 24 hour SBP > 15 mm Hg lower than the office SBP and 24 hour mean DBP > 10 mm Hg lower than the office DBP) was excluded.

A total of 92 subjects met the above criteria for the value of SBP and DBP; of these, 16 were excluded due to white-coat syndrome — 76 curves were then assessed (Table 1). Office BP was measured with a calibrated mercury sphygmomanometer, with an accuracy of 2 mm Hg; ABPM

Table 1. Sample group

	Number of	
	subjects	
Assessed ABPM	832	
Office SBP 128–132 mm Hg and DBP 78–82 mm Hg	92	
White coat syndrome	16	
Assessed ABPM	76	

ABPM — ambulatory blood pressure monitoring; DBP — diastolic blood pressure; SBP — systolic blood pressure

was measured by the SpaceLabs 90207 device (Redmond, WA, USA), both according to the criteria of the ESH. BP and heart rate (HR) during ABPM were measured every 15 min from 06:00 to 22:00 hours, and every 30 min from 22:00 to 06:00 hours. ABPM records had to contain at least 50 valid BP measurements in 24 hours, and all had to have hourly averages available. The mean 24 hour BP, awake BP and asleep BP were identified according to the records kept about the time of falling asleep and the time of waking. MAP was calculated using the formula: MAP = DBP + (SBP – DBP) \times 3⁻¹; PP was calculated as: PP = SBP – DBP.

Statistical analysis

Mean \pm standard deviation was calculated, as were the $5^{th}-95^{th}$ percentiles of the resulting median values of ABPM. The correlation between office BP and ABPM was calculated using Pearson's correlation. The results were rounded up to one decimal place because hundredths are of no importance in terms of BP in clinical practice. BP percentiles were evaluated as whole numbers. Microsoft Excel version 2007 and IBM SPSS Statistics Version 19 were used for statistical processing. The study was approved by an institutional review committee and was conducted in accordance with the Helsinki Declaration [9]. The subjects on the study gave informed consent.

RESULTS

The characteristics of the sample group and anthropometric parameters are shown in Table 2.

The data of the sample (n = 76) with office SBP 128–132 mm Hg and DBP 78–82 mm Hg (office BP, ABPM,

Table 2. Characteristics of sample group with office systolic blood pressure 128–132 mm Hg and diastolic blood pressure 78–82 mm Hg

	Males and females ($n = 76$)	Males (n = 40)	Females (n = 36)
Age [years]	55.6 ± 8.3	54.9 ± 9.3	56.0 ± 6.9
Height [m]	172.4 ± 8.7	179.0 ± 6.1	165.8 ± 5.4
Weight [kg]	78.3 ± 10.1	83.9 ± 7.5	72.1 ± 8.5
BMI [kg/m²]	26.2 ± 2.8	26.1 ± 2.1	26.3 ± 3.3
Smoking [%]	30	33	28

BMI — body mass index

Table 3. Office blood pressure 128-132 mm Hg and 78-82 mm Hg and corresponding ambulatory blood pressure parameters

BP [mm Hg]	Males and females	Males	Females	
HR [/min]	(n = 76)	(n = 40)	(n = 36)	
Office SBP	129.8 ± 1.6	129.9 ± 1.8	129.7 ± 1.7	
Office DBP	80.3 ± 1.5	80.2 ± 1.7	80.3 ± 1.4	
Office HR	75.6 ± 6.8	75.6 ± 6.9	76.2 ± 6.8	
Office MAP	96.8 ± 1.3	96.7 ± 1.8	96.8 ± 1.4	
Office PP	49.5 ± 1.9	49.4 ± 1.7	49.7 ± 2.2	
24 hour SBP	121.9 ± 2.0	122.3 ± 1.8	121.5 ± 2.1	
5 th –95 th percentile 24 h SBP	119–128	119–128	118–128	
24 h HR	73.9 ± 8.1	74.3 ± 8.8	73.5. ± 7.2	
Awake SBP	124.9 ± 2.4	125.4 ± 2.3	124.4 ± 2.3	
5 th –95 th percentile awake SBP	121–129	121–129	120–129	
Awake HR	77.4 ± 9.1	77.2 ± 9.6	77.5 ± 8.4	
Asleep SBP	109.1 ± 3.9	109.2 ± 3.3	109.0 ± 4.5	
5 th –95 th percentile asleep SBP	101–115	102–116	100–116	
Asleep HR	64.3 ± 7.6	63.9 ± 7.4	64.9 ± 7.9	
24 hour DBP	73.1 ± 1.9	73.3 ± 1.8	73.0 ± 2.1	
5 th –95 th percentile 24 h DBP	70–78	71–78	69–78	
Awake DBP	75.5 ± 2.2	75.5 ± 2.0	75.5 ± 2.4	
5 th –95 th percentile awake DBP	71–79	72–80	71–79	
Asleep DBP	63.3 ± 4.0	63.9 ± 4.3	62.5 ± 3.5	
5 th –95 th percentile asleep DBP	54–68	55–71	55–68	
24 hour MAP	89.4 ± 1.5	89.6 ± 1.3	89.2 ± 1.6	
5 th –95 th percentile 24 h MAP	87–94	88–94	87–94	
24 hour PP	48.8 ± 2.7	49.1 ± 2.6	48.5 ± 2.8	
5 th –95 th percentile 24 h PP	43–54	44 – 54	43–54	
Awake MAP	92.0 ± 1.7	92.1 ± 1.8	91.8 ± 1.8	
5 th –95 th percentile awake MAP	88–96	89–96	88–95	
Awake PP	49.5 ± 3.0	49.9 ± 2.7	48.9 ± 3.2	
5 th –95 th percentile awake PP	44–55	44–54	43–56	
Asleep MAP	78.6 ± 3.5	79.0 ± 3.4	78.0 ± 3.5	
5 th –95 th percentile asleep MAP	73–85	72–86	70–83	
Asleep PP	45.9 ± 4.0	45.3 ± 4.2	46.5 ± 3.5	
5 th –95 th percentile asleep PP	39–52	39–53	41–51	

BP — blood pressure; SBP — systolic blood pressure; DPB — diastolic blood pressure; HR — heart rate; MAP — mean arterial pressure; PP — pulse pressure; 5th—95th — 5–95th percentiles of median 24 hour ambulatory blood pressure monitoring value

5th – 95th percentiles, heart rate and Pearson's correlation between office BP and ABPM) is shown in Tables 3 and 4.

The mean values of ABPM corresponding to an office BP of 130 mm Hg SBP and 80 mm Hg DBP with $5^{th}-95^{th}$ percentiles are shown in Table 5.

DISCUSSION

Mean BP values during ABPM are lower than office BP. This is due to stress induced by the hospital environment when measuring office BP, and the physiological decrease

in BP during sleep, which reduces the overall mean value of ABPM. In practical terms, the ABPM record provides more information about the subject than a single measurement of BP at the clinic. BP is a fluctuating and volatile variable, and larger numbers of measurements reduce the likelihood of error during recording of extreme BP oscillations. ABPM allows the assessment of BP when the subject is awake and asleep, and at crucial times during the day (morning and late afternoon increase in BP). Office BP target values are set arbitrarily on the basis of the results of large population

Table 4. Pearson's correlation between office and 24 hour ambulatory blood pressure

Pearson's correlation (n = 76)	Office SBP correlation (95% CI)	Significance (two-tailed)
24 hour SBP	0.170 (-0.078-0.415)	0.141*
Awake SBP	0.119 (-0.129-0.378)	0.304*
Asleep SBP	0.144 (-0.092-0.373)	0.213*
Pearson's correlation (n = 76)	Office DBP correlation (95% CI)	Significance (two-tailed)
Pearson's correlation (n = 76) 24 hour DBP	Office DBP correlation (95% CI) 0.202 (-0.051-0.415)	Significance (two-tailed) 0.080*

SBP — systolic blood pressure; DPB — diastolic blood pressure; CI — confidence interval; *value is not statistically significant

Table 5. Mean and 5th-95th percentiles of 24 hour ambulatory blood pressure monitoring (ABPM) values corresponding to office blood pressure value of 130 and 80 mm Hg

ABPM [mm Hg]	24 hour		Awake		Asleep	
N = 76	Mean	5 th -95 th	Mean	5 th -95 th	Mean	5 th -95 th
Systolic blood pressure	122	119–128	125	121–129	109	101–115
Diastolic blood pressure	73	70–78	76	71–79	63	54–68

5th–95th — 5th–95th percentiles of median ABPM value

studies. The 2009 Reappraisal of the European guidelines on hypertension management, as if foreseeing the results of the ACCORD Blood Pressure study, recommended target SBP levels of 130-139 mm Hg for patients with diabetes, consistent with results of the ADVANCE study [3, 10, 11]. The ACCORD study sought to determine whether a decrease in SBP to < 120 mm Hg would result in a greater reduction in the incidence of cardiovascular complications compared to a decrease in SBP to < 140 mm Hg. A decrease in SBP to < 120 mm Hg (mean BP during therapy 119.3/64.4 mm Hg) did not result in a significant decrease in the composite primary end-point (nonfatal myocardial infarction, nonfatal stroke, and cardiovascular mortality) or a decrease in cardiovascular or total mortality compared to standard therapy (mean BP during therapy 133.5/70.5 mm Hg). However, there was a significant decrease in the incidence of stroke in the group with target systolic BP < 120 mm Hg. Signs of renal dysfunction were also favourably affected in the group achieving intensive SBP control [11]. Nor did the results of the Cardio-Sis study support a lower BP goal than is recommended at present in non-diabetic patients with hypertension. In this randomised open-label trial undertaken in 44 centres in Italy, 1,111 non-diabetic patients with SBP 150 mm Hg or greater were randomly assigned to a target SBP of less than 140 mm Hg (usual control; n = 553) or less than 130 mm Hg (tight control; n = 558). The primary end-point was the rate of electrocardiographic left ventricular hypertrophy two years after randomisation. Over a median follow-up of two years, the primary end-point occurred in 17.0% in the usual-control group (< 140 mm Hg) and in

11.4% of the tight-control group (< 130 mm Hg) (odds ratio 0.63; 95% CI 0.43–0.91; p = 0.013). A composite cardiovascular end-point occurred in 9.4% patients in the usual-control group and in 4.8% in the tight-control group (hazard ratio 0.50; 95% CI 0.31–0.79; p = 0.003). This clearly suggests the benefit of lowering SBP < 130 mm Hg in non-diabetic patients with uncomplicated hypertension [12].

Hence, there is no rationale for decreasing SBP $< 130 \, \text{mm} \, \text{Hg}$ in all patients with type-2 diabetes mellitus in terms of total and cardiovascular mortality. In patients at high risk for stroke, i.e. primarily elderly patients and individuals after a stroke, it is advisable to decrease SBP to < 130 mm Hg [3, 11]. Mean ABPM target values are set on the basis of population studies that compare office BP and ABPM. Target values differ slightly among authors and studies, which might be due to a number of circumstances, such as a different number of measurements during the day and the night, the age of subjects (young vs. old), different criteria for the white-coat syndrome and masked hypertension, and possible non-exclusion of this data from the statistical evaluation etc. Most existing data represents ABPM values corresponding to an arbitrary office BP value of 140/90 mm Hg. Only some of the data corresponds to different stages of hypertension according to the ESH and to the target BP value of 130-139/80-85 mm Hg [7, 8]. A possible exception is the PAMELA study, in which Italian researchers examined 1,438 subjects aged 24–66 years without antihypertensive medication and found a mean office BP value of 128/82 mm Hg, which corresponds to the mean values of 24 hour ABPM (118/74 mm Hg), awake ABPM (123/79 mm Hg) and asleep ABPM (108/65 mm Hg) [13]. One

group of these subjects were hypertensive and another group had an office BP significantly < 130/80 mm Hg.

Our work recorded the values for treated hypertensive patients. The average age of about 55 years was chosen because it marks the beginning of a significant increase in the prevalence of hypertension, type 2 diabetes and CVD in the Czech population [14]. We also calculated the relationship between office and ambulatory BP levels. According to Pearson's coefficient, we did not find out this relationship in our sample (Table 4). This is probably due to the very tight range of office BP levels (128–132 and 78–82 mm Hg) with a low value of standard deviation as opposed to a wide range of ABPM BP levels. Therefore we could not set that office and ABPM data are dependent.

Because ABPM reflects many aspects of BP (i.e. diurnal rhythm, morning surge, physical and psychosocial activity and many others) it should be very cautiously compared to office values. In our sample group, the mean values of ABPM relating to an office BP of 130 mm Hg SBP and 80 mm Hg DBP were (1) SBP: 24 hour, 122 mm Hg (5th – 95th percentiles, 119–128 mm Hg); awake, 125 mm Hg (5th – 95th percentiles, 121–129 mm Hg); and asleep, 109 mm Hg (5th – 95th percentiles, 101–115 mm Hg); (2) DBP: 24 hour, 73 mm Hg (5th – 95th percentiles, 70–78 mm Hg); awake, 76 mm Hg (5th – 95th percentiles, 71–79 mm Hg); and asleep, 63 mm Hg (5th – 95th percentiles, 54–68 mm Hg) (Tables 3, 5) 5th – 95th percentiles of BP values were included in the calculation, which allows some variation above the average values of BP.

CONCLUSIONS

The target values of ABPM identified in this study can be used in clinical practice and will contribute to risk stratification and treatment of hypertension. Further, they will enable specialists and general practitioners to assess the ABPM value in patients with an office BP about 130/80 mm Hg.

Acknowledgements

This study was supported by a grant from the Ministry of Education, Youth and Sports of the Czech Republic, No. MSM0021622402.

Conflict of interest: none declared

References

- Widimsky J, Cifkova R, Spinar J et al. Recommendation of Diagnostic Evaluation and Treatment of High Blood Pressure 2007. Czech Society of Hypertension. Vnitr Lek 2008; 54: 101–118.
- Mancia G, De Backer G, Dominiczak A et al. 2007 Guidelines for the management of arterial hypertension. The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens, 2007; 25: 1105–1187.
- Mancia G, Laurent S, Agabiti-Rosei E at al. Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document. J Hypertens, 2009; 27: 2121–2158.
- Mancia G, Parati G. Ambulatory blood pressure monitoring and organ damage. Hypertension, 2000; 36: 894–900.
- Verdecchia P. Prognostic value of ambulatory blood pressure: Current evidence and clinical implications. Hypertension, 2000; 35: 844–852.
- 6. NICE clinical guideline 127 Hypertension: clinical management of primary hypertension in adults. www.nice.org.uk/guidance/CG127.
- Bur A, Herkner H, Vlcek M et al. Classification of blood pressure levels by ambulatory blood pressure in hypertension. Hypertension, 2002; 40: 817–822.
- Head GA, McGrath BP, Mihailidou AS et al. Ambulatory blood pressure monitoring in Australia: 2011 consensus position statement. J Hypertens, 2012; 30: 253–266.
- 41st World Medical Assembly. Declaration of Helsinki: recommendations guiding physicians in biomedical research involving human subjects. Bull Pan Am Health Organ, 1990; 24: 606–609.
- ADVANCE Collaborative Group. Effects of a fixed combination
 of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the
 ADVANCE trial): a randomised controlled trial. Lancet, 2007;
 370: 829–840.
- The ACCORD Study Group. Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus. The ACCORD Study Group. N Engl J Med, 2010; 362: 1575–1585.
- Verdecchia P, Staessen JA, Angeli F et al. Usual versus tight control of systolic blood pressure in non-diabetic patients with hypertension (Cardio-Sis): an open-label randomised trial. Lancet, 2009; 374: 525–533.
- Mancia G, Sega R, Bravi C et al. Ambulatory blood pressure normality: results from the PAMELA study. J Hypertens, 1995; 13: 1377–1390.
- Cifkova R, Skodova Z, Lanska et al. Trends in blood pressure levels, prevalence, awareness, treatment, and control of hypertension in the Czech population from 1985 to 2000/01. J Hypertens, 2004; 22: 1479–1485.

Wartości uzyskane w całodobowym automatycznym pomiarze ciśnienia tętniczego odpowiadające wartości ciśnienia tętniczego zmierzonej w gabinecie lekarskim wynoszącej 130/80 mm Hg

Ivan Rihacek¹, Petr Frana¹, Martin Plachy¹, Bohuslav Kianicka¹, Miroslav Soucek¹, Anna Vasku²

Streszczenie

Wstęp: Dotychczas nie przedstawiono danych dotyczących wartości uzyskanych w całodobowym automatycznym pomiarze ciśnienia tętniczego (ABPM) u chorych, u których ciśnienie tętnicze zmierzone w gabinecie lekarskim wynosiło 130/80 mm Hg.

Cel: Celem badania było ustalenie, jakie wartości ciśnienia tętniczego w ABPM u chorych z nadciśnieniem tętniczym stosujących leki przeciwnadciśnieniowe odpowiadają wynikowi pomiaru gabinetowego wynoszącego 130/80 mm Hg.

Metody: Przeprowadzono pomiary ciśnienia tętniczego u osób w wieku 40–70 lat, stosując ABPM i gabinetowy pomiar sfigmomanometrem rtęciowym. Kryterium włączenia do badania było uzyskanie w pomiarze gabinetowym średniej wartości ciśnienia skurczowego (SBP) 128–132 mm Hg i rozkurczowego (DBP) 78–82 mm Hg. Kryteria włączenia spełniło 76 osób.

Wyniki: Średnie wartości w gabinetowych pomiarach ciśnienia tętniczego wynosiły: SBP 129,5 \pm 1,1 mm Hg, DBP 79,9 \pm 1,3 mm Hg. W pomiarach za pomocą ABPM uzyskano następujące wartości: SBP 121,9 \pm 2,0 mm Hg, DBP 73,1 \pm 1,9 mm Hg. Średnie ciśnienie tętnicze w porze aktywności dziennej wynosiło: SBP 124,9 \pm 2,4 mm Hg, DBP 75,5 \pm 2,2 mm Hg, a w porze nocnej — SBP 109,1 \pm 3,9 mm Hg, DBP 63,3 \pm 4,0 mm Hg.

Wnioski: Uzyskane w niniejszym badaniu wartości ciśnienia tętniczego zmierzone w ABPM mogą być użyteczne w praktyce klinicznej i przyczynią się do poprawy stratyfikacji ryzyka oraz leczenia nadciśnienia tętniczego.

Słowa kluczowe: badanie populacyjne, pomiar ciśnienia tętniczego, gabinetowe ciśnienie tętnicze 130/80 mm Hg, automatyczny pomiar ciśnienia tętniczego, odpowiadające ciśnienie tętnicze

Kardiol Pol 2013; 71, 7: 675-680

Adres do korespondencji:

Ivan Rihacek, MD, PhD, 2nd Internal Department, University Hospital St. Anna, Pekarska 53, 65691 Brno, Czech Republic, tel: +420543182236, fax: 5431822312, e-mail: ivan rihacek@fnusa.cz

Praca wpłynęła: 17.07.2012 r. Zaakceptowana do druku: 05.12.2012 r.

¹2nd Internal Department, University Hospital St. Anna and Masaryk University, Brno, Czechy

²Department of Pathological Physiology, Masaryk University, Brno, Czechy