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REPRODUCIBILITY OF THE CAROTID INTIMA-MEDIA THICKNESS, BAROREFLEX SENSITIVITY, AND VARIABILITY IN BLOOD PRESSURE AND HEART RATE IN NORMOTENSIVES AND HYPERTENSIVES

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Abstract

Reproducibility of the relationship between carotid intima-media thickness (IMT) and baroreflex sensitivity (BRS) was studied in normotensives and hypertensives with respect to the signs of tonic and reflex autonomic control of heart rate and blood pressure (BP).

We studied 25 treated hypertensives (Hy; 49±10 years) and 15 healthy controls (Norm; 44±9 years) twice in a period of one year. IMT was determined ultrasonographically. From the 5-minute beat-to-beat recordings of BP (Finapres) the following items were determined: baroreflex sensitivity by the spectral method as BRS (in ms/mmHg) and BRSf (in mHz/mmHg), short-term variability of inter-beat intervals (IBI), and systolic and diastolic BP (SBP and DBP) as standard deviations (IBIsd, SBPsd, DBPsd), and by the spectral method as the spectral power at a frequency of 0.1 Hz (in absolute units – vSBPabs, vDBPabs, vIBIabs, and in relative units – vSBPrel, vDBPrel, vIBIrel). Twenty-four-hour variability of SBP, DBP, and IBI was derived from 24-hour recordings of BP and ECG as a difference in day and night values and as ASDNN and SDANN indices.

After one year, SBP measured by Finapres decreased by 9 mmHg ($p<0.05$) in normotensives. In hypertensives, BP values decreased when measured by 24-hour monitoring – DBP during day by 4 mmHg ($p<0.05$), mean DBP in 24h by 3 mmHg ($p<0.05$), and by Finapres as well – SBP by 13 mmHg ($p<0.01$), DBP by 12 mmHg ($p<0.05$), variability of SBPsd decreased by 1 mmHg ($p<0.05$), of DBPsd by 0.5 mmHg, ($p<0.05$), but the variability vSBPrel increased by 0.023 r.u. ($p<0.05$). In patients, SDANN (24h index variability of IBI) decreased by 22 ms ($p<0.01$). Other parameters were unchanged after one year.

A decrease of BP, a decrease of short-term blood-pressure variability, and a shift of the power in the spectra of SBP in the range of 0.1 Hz could be regarded as a positive effect of the therapy.

Key words

Carotid intima-media thickness, Baroreflex sensitivity, Heart rate variability, Blood pressure variability, Reproducibility

Abbreviations used

ASDNN, the mean of standard deviations of RR intervals determined in 5-minute periods of 24-hour ECG; BMI, body mass index; BP, blood pressure; BRS, baroreflex sensitivity in ms/mmHg; BRSf, baroreflex sensitivity in mHz/mmHg; DBP, diastolic blood pressure; DBPsd, standard deviation

of diastolic blood pressure determined from the 5-minute beat-to-beat recordings; DBPd-n, day-night difference of DBP determined from the 24h blood pressure monitoring; DBPd, mean of diastolic blood pressure determined for the day period of 24h monitoring; DBPn, mean of diastolic blood pressure determined for the night period of 24h monitoring; DBP24h, mean of diastolic blood pressure determined from the 24h monitoring; ECG, electrocardiogram; HR, heart rate; HRd, mean of heart rate determined for the day period of 24h monitoring; HRn, mean of heart rate determined from the night period of 24h monitoring; HR24h, mean of heart rate determined from the 24h monitoring; Hy, group of hypertensives; IBI, inter-beat interval (ms); IBIsd, standard deviation of inter-beat intervals determined from the 5-minute beat-to-beat recordings of blood pressure; IMT, intima-media thickness; MAPd, averaged values of mean arterial pressure determined for the day period of 24h monitoring, MAPn, averaged values of mean arterial pressure determined for the night period of 24h monitoring; MAP24h, averaged values of mean arterial pressure from the 24h monitoring; Norm, group of healthy controls; RR interval, heart period from ECG; SBP, systolic blood pressure; SBPsd, standard deviation of systolic blood pressure determined from the 5-minute beat-to-beat recordings; SBPd-n, day-night difference of SBP determined from 24h blood pressure monitoring; SBPd, mean of systolic blood pressure determined for the day period of 24h monitoring; SBPn, mean of systolic blood pressure determined for the night period of 24h monitoring; SBP24h, mean systolic blood pressure determined from 24hour monitoring; SDANN, standard deviation of mean RR intervals determined in 5-minute periods in 24h ECG; vDBPabs, variability of diastolic blood pressure determined as spectral power at a frequency of 0.1 Hz (in mmHg2/Hz) from the 5-minutes´ beat-to-beat recordings of blood pressure; vDBPrel, variability of diastolic blood pressure determined as spectral power at a frequency of 0.1 Hz (in relative units) from the 5-minute beat-to-beat recordings of blood pressure; vIBIabs, variability of inter-beat interval determined as spectral power at a frequency of 0.1 Hz (in ms2/Hz) from the 5-minute beat-to-beat recordings of blood pressure; vIBIrel, variability of inter-beat interval determined as spectral power at a frequency of 0.1 Hz (in relative unit) from the 5-minute beat-to-beat recordings of blood pressure; vSBPabs, variability of systolic blood pressure determined as spectral power at a frequency of 0.1 Hz (in mmHg2/Hz) from the 5-minute beat-to-beat recordings of blood pressure; vSBPrel, variability of systolic blood pressure determined as spectral power at a frequency of 0.1 Hz (in relative unit) from the 5-minute beat-to-beat recordings of blood pressure

INTRODUCTION

Essential hypertension is a multifactor disease which is linked with changes of autonomous regulation of circulation, especially increased sympathetic activity. Due to a stiffening of the carotid wall, determined by an increase of its intima media thickness (IMT) (*1, 2*), the reflex response to blood pressure variations, e.g. baroreflex sensitivity, is diminished (*3*). The baroreflex is one of the basic mechanisms regulating blood pressure (BP). It has not only a long-lasting effect on the mean BP, but it also damps short-term variations in BP through autonomic adjustments in heart rate, cardiac output, and peripheral resistance (*4,5*). From this complex control response usually regulated by baroreflex, the baroreflex sensitivity (BRS) is studied, which is defined as the change of the inter-beat interval (IBI) due to the change of systolic BP (*6*), in some studies BRSf as the change of the heart rate (HR) due to the change of systolic BP (*3, 7*). That means that beside the increased sympathetic activity, the parasympathetic activity is suppressed in hypertensives. This is of high clinical importance, because the decreased parasympathetic activity quantified as a low BRS and low values of indices of heart rate variability, increases the risk of sudden cardiac death after myocardial infarction (*8,9).*

The reproducibility of complex involvement of changes of IMT in autonomous regulation of heart rate and BP in healthy subjects and hypertensives is not known. The aim of the present study was to test reproducibility of IMT, baroreflex sensitivity and variability of blood pressure and heart rate after a one-year interval in normotensive subjects and hypertensive patients.

METHODS AND SUBJECTS

We studied 25 treated hypertensives (Hy; 10 men and 15 women; mean±SD: age 49±10 years, body height 172.6±10.4 cm, weight 78.4±12.8 kg, body mass index – BMI 26.2±3.1 kg/m^2) and 15 healthy controls (Norm; 6 men and 9 women; age 44±9 years, body height 169.7±7.0 cm, weight 72.6±14.8 kg, BMI 25.1±4.3 kg/m^2). There were no significant differences between both groups in baseline characteristics. Patients with hypertension were recruited randomly from the outpatient Departments of Internal Cardiology of the Faculty Hospital in Brno. All patients had mild-to-moderate essential hypertension and had no history or evidence of left ventricular dysfunction, previous myocardial infarction, stroke, or diabetes mellitus. The diagnosis of hypertension was established by the presence of an increase in BP (≥140 mmHg systolic and ≥90 mmHg diastolic BP) and the absence of clinical or laboratory evidence suggestive of secondary forms of hypertension. Hypertension was diagnosed as sustained on the basis of several BP measurements made successively by the general practitioner referring the patient to the Faculty Hospital in Brno.

Predictably, all patients were receiving blood-pressure lowering medications and some also lipid-lowering medications with cardiovascular effects. These included: diuretics (n=11), calcium channel blockers (n=8), angiotensin-converting enzyme inhibitors (n=13), beta-blockers (n=18), and statins (n=3). Discontinuation of medications for the purpose of this study was not justified.

Control subjects were recruited from volunteers at the Department of Internal Cardiology and the Department of Physiology. All subjects gave their informed consent, and the protocols were approved by the ethics committee. The following measurements were done twice in a period of one year.

Determination of the carotid intima-media thickness

Carotid intima-media thickness was determined ultrasonographically (Agilent Sonos 5500, Philips). B-mode ultrasonography (3–11 MHz high-resolution transducer) was performed with all subjects in supine position with the neck extended in mild rotation. The measurements were performed on both the right and the left common carotid artery. The artery was examined on a far wall from the transducer at a distance of 1 cm proximally from the transition of the a. carotis communis into the bulbus. Five measurements in this position were performed (sections of 2 mm) twice by the same physician and an average of these measurements was calculated. Subsequently, we took this average value and determined the mean value of both (together a. carotis dextra and a. carotis sinistra) as an average IMT.

Ambulatory blood pressure and ECG monitoring

Ambulatory blood pressure monitoring was carried out by a Tonoport IV device (Marquette Hellige). The cuff was placed on the non-dominant arm. The device was programmed to take one blood pressure measurement every 20 min (daytime) or every 40 min (night-time). The time at which the device was applied was the same (±1 h) in all patients. The recording was then analysed to obtain day-time (from 6 a.m. to 9 p.m. hours), and night-time (from 10 p.m. to 5 a.m. hours) average mean, systolic and diastolic blood pressures (MAPd, MAPn, MAP_{24h}, SBPd, SBPn, SBP_{24h}, DBPd, DBPn, DBP_{24h}) and heart rate (HRd, HRn, HR_{24h}), and also the difference between day and night values of blood pressure (MAPd-n, SBPd-n, DBPd-n).

A two-channel, 24-hour ECG recording was performed (SeerMC Marquette, Hellige). Two non-spectral indices of heart rate variability were computed: the SDANN index – the standard deviation of

mean RR intervals determined in 5-minute periods in 24 hours, and the ASDNN index – the mean of standard deviations of RR intervals determined in 5-minute periods in 24 hours.

Short-term variability in blood pressure and inter-beat intervals, and baroreflex sensitivity determination

We recorded IBI, SBP, and DBP beat-to-beat, on finger arteries by the Peňáz non-invasive method (Finapres OHMEDA, USA) in all subjects. The recordings were taken in sitting position at rest during a 5-minute period. Breathing was synchronised by a metronome at 20 breaths per minute (0.33 Hz) and the subjects were allowed to adjust the tidal volume according to their own comfort. The power spectra of variability of IBI, SBP and DBP, and cross-spectra between IBI and SBP were calculated. Short-term variability in these variables was determined as standard deviations (IBIsd, SBPsd, DBPsd), and by the spectral method as the spectral power at a frequency of 0.1 Hz (in absolute and relative units – vSBPabs, vDBPabs, vIBIabs, vSBPrel, vDBPrel, vIBIrel). The gain factors between variations in SBP and IBI, or instantaneous values of heart rate respectively, were calculated at a frequency of 0.1 Hz (10) and taken as a measure of baroreflex sensitivity (index BRS in ms/mmHg and index BRSf in mHz/mmHg).

Statistics

The individual data from the examinations were continuously saved in the table processors – Excel and Statgraphics. The differences between the values of all parameters in hypertensives and normotensives were evaluated, and their reproducibility after one year as well. The reproducibility of dependence of IMT on age, and BRS on IMT, was determined. The significance of differences and correlations was evaluated by the Mann-Whitney test and Spearman's correlation coefficient.

RESULTS

The differences between cardiovascular parameters of the two groups, hypertensives and normotensives, and their reproducibility after one year are presented in *Table 1.* Characteristic signs of increased sympathetic and decreased parasympathetic control of circulation were present in both measurements in a period of one year, IMT was significantly increased in patients with hypertension ($p<0.01$), and baroreflex sensitivity measured by both indices (BRS and BRSf) was significantly lower in hypertensives ($p<0.01$ or $p<0.05$). As to variability in heart rate and blood pressure, during this repeated measurement a characteristic decrease in variability of IBI and DBP at 0.1 Hz were present. After one year, SBP measured by Finapres decreased by 9 mmHg ($p<0.05$) in normotensives. In hypertensives, BP values decreased when measured by 24-hour monitoring – DBP during day by 4 mmHg ($p<0.05$), mean DBP in 24h by 3 mmHg ($p<0.05$), and by Finapres as well – SBP by 13 mmHg ($p<0.01$), DBP by 12 mmHg ($p<0.05$), variability of SBPsd decreased by 1 mmHg ($p<0.05$), that of DBPsd by 0.5 mmHg, ($p<0.05$), but the variability SBPrel increased by 0.023 r.u. ($p<0.05$). The 24h index variability of IBI – SDANN decreased by 22 ms ($p<0.01$). Other parameters were unchanged after one year. Correlations between IMT and age, and BRS and IMT, were also reproducible (*Fig. 1*).

DISCUSSION

Our study confirmed that IMT in hypertensives is greater than in normotensives together with a suppression of BRS and BRSf and a dampening of the short-term heart rate variability (*1, 2, 3, 11*).

Even though many studies compare the influence of methodology of BRS determination (*12, 13*) on BRS values, there are few studies on the reproducibility of power spectra (*14*) or BRS (15). This study proved the reproducibility of intima-media thickness, baroreflex sensitivity, blood pressure, and short-term and 24h variability in blood pressure and heart rate in healthy subjects.

In hypertensives, intima-media thickness, baroreflex sensitivity, and the short-term heart rate variability are also reproducible. Their decrease of blood pressure, the decrease of short-term blood-pressure variability, and the increase of the relative power in the spectra of SBP in the range of 0.1 Hz could be regarded as a positive effect of the therapy.

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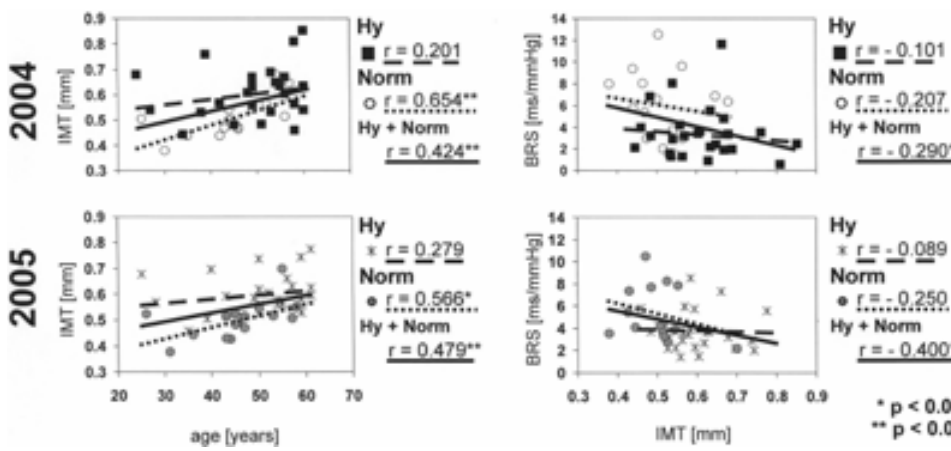

Fig. 1.
Correlation between intima-media thickness and age, and baroreflex sensitivity and IMT in normotensives and hypertensives

Legends: IMT – intima-media thickness, BRS – baroreflex sensitivity, r – Spearman's correlation coefficient, Hy – group of hypertensives, Norm – group of normotensives, Hy+Norm – both groups together, description of markers and lines – see *Fig. 1*

Table 1
Reproducibility of differences between cardiovascular parameters in normotensives and hypertensives (2004/2005)

PARAMETERS	NORMOTENSIVES	HYPERTENSIVES	p level: Norm vs. Hy
INTIMA-MEDIA THICKNESS			
IMT (mm)	0.52 ± 0.08 / 0.50 ± 0.07	0.61 ± 0.10 / 0.60 ± 0.08	p < 0.01 / p < 0.001
24h BLOOD PRESSURE MONITORING			
HR_{24h} (bpm)	82 ± 6 / 80 ± 6	79 ± 7 / 80 ± 6	NS / NS
SBP_{24h} (mmHg)	115 ± 7 / 119 ± 8	128 ± 8 / 125 ± 10	p < 0.001 / p < 0.05
DBP_{24h} (mmHg)	76 ± 6 / 78 ± 6	81 ± 7 / 78 ± 7*	p < 0.05 / NS
MAP_{24h} (mmHg)	89 ± 6 / 91 ± 6	97 ± 7 / 94 ± 7*	p < 0.001 / NS
HRd (bpm)	83 ± 7 / 82 ± 7	81 ± 7 / 81 ± 6	NS / NS
SBPd (mmHg)	117 ± 9 / 120 ± 9	130 ± 8 / 128 ± 10	p < 0.001 / p < 0.01
DBPd (mmHg)	77 ± 9 / 80 ± 7	84 ± 8 / 80 ± 8*	p < 0.05 / NS
MAPd (mmHg)	90 ± 9 / 93 ± 8	99 ± 7 / 96 ± 7*	p < 0.001 / NS
HRn (bpm)	75 ± 6 / 75 ± 5	73 ± 5 / 75 ± 6	NS / NS
SBPn (mmHg)	105 ± 9 / 109 ± 12	117 ± 10 / 115 ± 11	p < 0.001 / NS
DBPn (mmHg)	68 ± 7 / 70 ± 7	74 ± 7 / 72 ± 8	p < 0.01 / NS
MAPn (mmHg)	80 ± 7 / 83 ± 8	89 ± 7 / 86 ± 7	p < 0.001 / NS
HRd-n (bpm)	7 ± 7 / 7 ± 7	8 ± 6 / 7 ± 5	NS / NS
SBPd-n (mmHg)	12 ± 9 / 12 ± 14	13 ± 9 / 13 ± 8	NS / NS
DBPd-n (mmHg)	9 ± 6 / 10 ± 9	9 ± 7 / 8 ± 7	NS / NS
MAPd-n (mmHg)	10 ± 6 / 10 ± 10	11 ± 7 / 10 ± 7	NS / NS
24h ECG MONITORING			
SDANN (ms)	137 ± 43 / 119 ± 41	140 ± 41 / 118 ± 32**	NS / NS
ASDNN (ms)	61 ± 20 / 56 ± 17	56 ± 16 / 57 ± 12	NS / NS
CONTINUOUS BLOOD PRESSURE MONITORING			
IBI (ms)	827 ± 91 / 815 ± 103	879 ± 195 / 897 ± 138	NS / p < 0.05
SBP (mmHg)	116 ± 18 / 108 ± 20*	131 ± 20 / 117 ± 23**	p < 0.05 / NS
DBP (mmHg)	66 ± 13 / 60 ± 12	74 ± 18 / 62 ± 14**	NS / NS
IBIsd (ms)	40 ± 20 / 36 ± 12	34 ± 35 / 30 ± 9	NS / NS
SBPsd (mmHg)	4.6 ± 1.2 / 6.1 ± 3.4	5.8 ± 1.9 / 4.8 ± 1.6*	p < 0.05 / NS
DBPsd (mmHg)	2.5 ± 0.5 / 2.9 ± 0.7	2.9 ± 0.9 / 2.4 ± 0.7*	NS / NS
vIBIabs (ms^2/Hz)	6284 ± 4851 / 7827 ± 5395	4193 ± 7288 / 2921 ± 2927	p < 0.05 / p < 0.001
vSBPabs ($mmHg^2$/Hz)	134 ± 128 / 179 ± 120	104 ± 124 / 118 ± 117	NS / NS
vDBPabs ($mmHg^2$/Hz)	55 ± 49 / 75 ± 45	39 ± 42 / 41 ± 47	NS / p < 0.01
vIBIrel (r.u.)	0.04 ± 0.02 / 0.05 ± 0.02	0.03 ± 0.02 / 0.03 ± 0.02	NS / p < 0.001

vSBPrel (r.u.)	0.05 ± 0.03 / 0.05 ± 0.03	0.02 ± 0.02 / 0.04 ± 0.03*	p < 0.05 / NS
vDBPrel (r.u.)	0.07 ± 0.05 / 0.07 ± 0.04	0.04 ± 0.03 / 0.05 ± 0.04	p < 0.05 / p < 0.05
BRS (ms/mmHg)	6.1 ± 3.1 / 5.3 ± 2.4	3.5 ± 2.5 / 3.8 ± 1.8	p < 0.01 / p < 0.05
BRSf(mHz/mmHg)	9.0 ± 4.4 / 8.2 ± 4.4	4.6 ± 2.6 / 6.1 ± 3.7	p < 0.01 / p < 0.01

The values are presented as mean±standard deviation. Legends: Abbreviations see in List of Abbreviations. Significance (Mann-Whitney test); year 2004 vs. 2005 – ** p< 0.01, * p< 0.05.

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REPRODUCIBILITA TLOUŠŤKY STĚN A. CAROTIS, CITLIVOSTI BAROREFLEXU A VARIABILITY KREVNÍHO TLAKU A TEPOVÉ FREKVENCE U NORMOTONIKŮ A HYPERTONIKŮ

S o u h r n

Cílem práce byla komplexní analýza reproducibility vztahů tloušťky stěny a. carotis (IMT) a citlivosti baroreflexu (BRS) u normotoniků a hypertoniků s ohledem na projevy tonického a reflexního autonomního řízení srdeční frekvence a krevního tlaku.

Vyšetřili jsme 25 léčených hypertoniků (Hy; 49±10 let) a 15 zdravých normotoniků (Norm; 44±9 let) dvakrát s odstupem jednoho roku. Echograficky jsme stanovili tloušťku stěny a. carotis (IMT). Z pětiminutového záznamu krevního tlaku (Finapres) jsme určili: citlivost baroreflexu spektrální metodou jako BRS (ms/mmHg) a BRSf (mHz/mmHg); krátkodobou variabilitu systolického a diastolického krevního tlaku (SBP, DBP) a tepových intervalů (IBI) jako standardní odchylku z pětiminutového záznamu (SBPsd, DBPsd, IBIsd); spektrální metodou jako výkon spektra při frekvenci 0.1 Hz (v absolutních a relativních jednotkách – vSBPabs, vDBPabs, vIBIabs, vSBPrel, vDBPrel, vIBIrel). Dvacetičtyřhodinová variabilita byla stanovena z 24h záznamů krevního tlaku (rozdíl denních a nočních hodnot: SBPd-n, DBPd-n) a EKG (indexy SDANN a ASDNN).

U kontrol klesl SBP měřený Finapresem o 9 mmHg (p<0,05). U hypertoniků klesl signifikantně DBPd o 4 mmHg (p<0,05), DBP_{24h} o 3 mmHg (p<0,05), variabilita v krevním tlaku SBPsd o 1 mmHg (p<0,05), DBPsd o 0,5 mmHg (p<0,05), krevní tlak z prstu SBP o 13 mmHg (p<0,01), DBP o 12 mmHg (p<0,05), 24h index variability IBI – SDANN o 22 ms (p<0,01), stoupla variabilita vSBPrel o 0,023 r.u. (p<0,05). Ostatní parametry byly po roce beze změny.

Pokles krevního tlaku, pokles krátkodobé variability tlaku a posun výkonu spektra SBP do pásma 0.1 Hz lze považovat za pozitivní výsledek léčby.

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