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Volume of carotid bodies and cardiac autonomic function in patients with essential hypertension

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ABSTRACT

Purpose: Determination of the relationship between the estimated total volume of the carotid bodies ($V_{rCB + lCB}$), assessed by computed tomography angiography (CTA), and the autonomic cardiac function in patients with essential hypertension (EH).
Materials and methods: The study included 69 patients with diagnosed and pharmacologically treated EH. The estimated volume of each carotid body (CB) was evaluated on the basis of scans obtained in the CTA of carotid arteries, using the following formula: 4/3 × π × half of transverse dimension of CB in axial projection × half of longitudinal dimension of CB in the axial projection × half of craniocaudal dimension of CB in the sagittal/coronal projection. Cardiac autonomic function was assessed using time domain analysis of heart rate variability (HRV).
Results: The mean values of SDNNi, rMSSD and pNN50 at 24-h monitoring, during daily activity and during night rest, were significantly lower in patients with hypertension with the values of $V_{rCB + lCB} \geq$ median compared to the group of hypertensive patients with the values of $V_{rCB + lCB} <$ median. Moreover, in patients with EH with the values of $V_{rCB + lCB} \geq$ median, the mean values of SDNN were lower during daily activity. Based on the regression analysis, it was found out that the higher values of $V_{rCB + lCB}$ are an independent risk factor in HRV reduction (expressed as a reduction in the rMSSD).
Conclusion: In patients with EH, a relationship between the volume of CB, assessed by CTA of carotid arteries, and autonomic cardiac function seems to be probable.

1. Introduction

Carotid bodies (CB) are small anatomic structures of maximum dimensions amounting to around 7 mm × 4 mm × 2 mm, situated on both sides, slightly posteriorly to division of common carotid artery into external and internal carotid arteries (Fitzgerald et al., 2009). The basic physiological function of carotid bodies involves chemical control of respiratory function (Ponikowski and Banasiak, 2001). In recent years, chemoreceptors of carotid bodies were demonstrated to play a significant role in control of cardiovascular system. Currently, literature of the topic devotes the highest attention to effects of chronically augmented activity of carotid bodies on the course of heart failure and arterial hypertension (Abdala et al., 2012; Niewiński et al., 2013; Paton et al., 2013; Ponikowski and Banasiak, 2001; Schultz et al., 2013). However, the determination of activity manifested by carotid bodies requires the application of poorly accessible electrophysiological methods. The most frequently employed electrophysiological method of measuring carotid bodies activity involves direct measurement of the reflective increase in muscle sympathetic nerve activity (MSNA) in response to short-term hypoxia or reflective decrease in MSNA as an effect of inhibition of peripheral chemoreceptors by hypoxia (Ponikowska et al., 2009).

On the basis of autopsy material, Sivridis et al., (2011) demonstrated a positive relationship between the hypertrophy of myocardium and the volume of carotid bodies. The studies seem to corroborate the hypothesis that the volume of carotid bodies could be related to the morphology and function of the cardiovascular system.

The development of imaging diagnostic techniques allows a reliable *in vivo* evaluation of the size of fine anatomic structures. In particular, the determination of carotid bodies' size became possible due to introduction to clinical practice of multi-slice computed tomography (Nguyen et al., 2011).

Arterial hypertension represents a recognised risk factor for the other cardiovascular diseases (Wolf-Maier et al., 2003; Zdrojewski et al., 2013). Abnormal control in autonomic system is one of cardiovascular complications in arterial hypertension and a marker of unfavourable prognosis or even an independent risk factor of sudden cardiac death. Heart rate

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variability (HRV) analysis provides a useful, non-invasive technique to evaluate cardiac autonomic function (ESC, 1996).

The fact of a lowered HRV was documented in patients with arterial hypertension, myocardial infarction, cardiomyopathies, heart rhythm disturbances and diabetes mellitus (Thayer et al., 2010; Xhyheri et al., 2012). Moreover, a favourable effect of cardiologic drugs has been suggested to depend on their effects on the autonomous system (Cloarec-Blanchard, 1997; Giles et al., 2001; Negrusz-Kawecka et al., 2004).

This study aimed at defining the relationship between the estimated total volume of the carotid bodies, assessed by computed tomography angiography (CTA), and autonomic function of the heart in patients with essential hypertension.

2. Materials and methods

2.1. Study population and protocol

The study was conducted on 69 consecutive individuals fulfilling inclusion criteria, i.e., age above 18 years, essential hypertension—diagnosed and pharmacologically treated for at least 5 years. The exclusion criteria included the following: secondary arterial hypertension (2 patients), diabetes mellitus (2), ischaemic heart disease (6), hypercholesterolaemia (7), hypertriglyceridaemia (9), renal insufficiency (2), hyperthyroidism (2) and hypothyroidism (1). Those criteria permitted to exclude 17 patients from the primary study group. Ten patients exhausted more than a single criterion of exclusion. Finally, a group of 52 patients suffering from essential hypertension, which was pharmacologically treated, has been constituted. Both carotid bodies could be visualised by CTA technique in 47 patients, forming the final investigated group. Clinical characteristics of the patients and characteristics of hypertension treatment applied in the group are shown in Table 1.

The written informed consent was obtained from all patients taking part in the study. The study was approved by the Local Ethics Committee.

In all qualified patients, the volume of carotid bodies and the cardiac autonomic function were evaluated. The estimated volume of each carotid body was evaluated on the basis of scans obtained in the computed tomography angiography (CTA) of carotid arteries. Cardiac autonomic function was assessed using time domain heart rate variability analysis (HRV).

Table 1
Clinical characteristics of hypotensive treatment in the study group.

Number	47
Age (years)	69.15 ± 11.32
Height (m)	1.68 ± 0.07
Body mass (kg)	71.77 ± 13.26
BMI (kg/m^2)	25.24 ± 3.22
Gender (%)	
Men	44.68
Women	55.32
Duration of arterial hypertension (years)	9.18 ± 4.22
Grades of arterial hypertension according to ESH/ECS (%)	
Mild	40.43
Moderate	46.81
Severe	12.76
Hypotensive Treatment (%)	100.00
Monotherapy	31.91
Combination Therapy	68.09
Hypotensive drugs (%)	100.00
ACE inhibitors	51.06
β-blockers	38.30
Diuretics	27.66
Calcium channel blockers	31.91
Angiotensin receptor blockers	23.40
Other hypotensive drugs	8.51

ACE—angiotensin-converting enzyme inhibitors; BMI—body mass index; ESC—European Society of Cardiology; ESH—European Society of Hypertension.

2.2. Criteria for selection of the study groups

Considering the median value of the estimated total volume of the carotid bodies, two groups of patients were distinguished: group A of patients suffering from essential hypertension, with estimated total volume of the carotid bodies ≥ median value ($n = 24$), and group B of patients suffering from essential hypertension with estimated total volume of the carotid bodies < median value ($n = 23$). At the subsequent stage of the studies, the accepted criterion of carotid body hypertrophy allowed to distinguish group C consisting of patients suffering from essential hypertension with hypertrophy of carotid bodies ($n = 6$) and group D of patients suffering from essential hypertension with normal total volume of the carotid bodies ($n = 41$). No significant differences were detected between groups A and B and between groups C and D in respect to clinical characteristics and characteristics of hypertension treatment.

2.3. CTA of carotid arteries

Studies of computed tomography angiography (CTA) of carotid arteries were conducted using SOMATOM Definition Dual-Source CT scanner (Siemens Healthcare, Germany), in line with the protocol dedicated to evaluation of carotid arteries in the arterial and delayed phases. In all studies included into the project, CTA studies were performed using a standardised protocol. In all CTA studies, the option of monitoring test bolus was used. Pre-monitoring scans were obtained at the level of aortic arch. Both in the arterial and the delayed phase acquisition progressed using the spiral technique, with colimation of 0.6 mm in the adcephalic direction from aortic arch to cerebral base, including arterial circle of Willis. The exposure was set at the level of 120 kV. In order to minimise radiation exposure, the function of Care Dose was used (Siemens Medical Solutions, Germany), which resulted in variable mAs values. An iodine, non-ionic contrast agent was used (100 ml in volume), administered to veins of cubital fossa at the rate of 4.5 ml/s. All studies were performed using Iomeprol contrast agent (Iomeron 400, Bracco UK Ltd, Great Britain), (Jaźwiec et al., 2013; Nguyen et al., 2011).

2.4. CB evaluation

Carotid bodies (CB) were evaluated on scans obtained in computed tomography angiography (CTA) of carotid arteries, Fig. 1. The quality of CB imaging, their anatomic position and the estimated volume of the CB were evaluated. The estimated volume of the CB (V_{CB}) was calculated assuming elliptic shape of CB, using the formula: $4/3 \times \pi \times$ half of transverse dimension of CB in axial projection $\times$ half of longitudinal dimension of CB in the axial projection $\times$ half of craniocaudal dimension of CB in the sagittal/coronal projection, Fig. 2. The dimensions were evaluated both on the right (rCB) and the left (lCB) side. The values of estimated total volume of the carotid bodies ($V_{rCB + lCB}$), presented in the study, represent sums of average volumes manifested by the right and the left carotid body obtained in two independent measurements conducted by two physicians-radiologists. The criterion of carotid body hypertrophy was accepted to involve values of estimated total volume of the carotid bodies ($V_{rCB + lCB}$) above 58.6 mm^3. The value of 58.6 mm^3 was obtained assuming that hypertrophy of carotid body involves dimensions of each carotid body exceeding maximum dimensions quoted in the literature, or $7 \times 4 \times 2$ mm.

2.5. Twenty-four-hour Holter monitoring and HRV analysis

In all persons who entered the study, 24-h Holter monitoring was performed using Lifecard CF recorder, and then the analysis using the