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Central *vs*. peripheral blood pressure components as determinants of retinal microvessel diameters

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Abstract *Background:* We assessed association of retinal arteriolar and venular diameters with central and peripheral blood pressure (BP).
Methods: We post-processed retinal photographs from 514 participants randomly recruited from a Flemish population (mean age, 50.6 years; 50.8% women), using IVAN software to generate retinal arteriolar (CRAE) and venular (CRVE) equivalents. We measured peripheral BP by mercury sphygmomanometry and central B*P* by tonometry at the carotid artery. We applied multivariable-adjusted regression analysis.
Results: For peripheral *vs*. central BP (mmHg) average levels were 126.6 *vs*. 122.1 systolic and 79.4 *vs*. 79.6 diastolic, and 95.1 *vs*. 97.9 and 47.2 *vs*. 42.5 for mean and pulse pressure, respectively. CRAE and CRVE averaged 153 μm and 219 μm. Effect sizes (μm) for CRAE for 1 − SD increase in peripheral *vs*. central BP were −3.77 *vs*. −3.52 systolic, −3.16 *vs*. −3.13 diastolic,

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−3.84 *vs.* −3.64 for mean BP, and −2.07 *vs.* −1.83 for pulse pressure ($p \leq 0.006$). Models that included two BP components demonstrated that CRAE decreased ($p \leq 0.035$) with systolic (peripheral *vs.* central, −2.87 *vs.* −2.40) and diastolic (−1.58 *vs.* −1.80) BP. CRAE decreased with mean BP (−3.53 *vs.* −3.53; $p < 0.0001$), but not with pulse pressure ($p \geq 0.19$). CRVE was not related to any peripheral or central BP component ($p \geq 0.062$). All CRAE regression slopes on corresponding peripheral and central BP components were similar ($p \geq 0.28$).
Conclusion: Higher systolic, diastolic and mean BPs were associated with smaller CRAE, regardless of whether BP was measured centrally or peripherally. Central BP does not refine the inverse association of CRAE and CRVE with peripheral BP.

Introduction

Non-mydriatic retinal photography allows the non-invasive assessment of the retinal micro-vessel in population studies.[1–9] The central retinal arteriolar equivalent (CRAE) and central retinal venular equivalent (CRVE) represent the average arteriolar and venular diameters in the retinal microvasculature.[10,11] Previous population studies established that CRAE decreases with higher blood pressure.[1–9] However, all of these studies relied on peripheral blood pressure as measured at the brachial artery.[1–9] Several reports suggested that central blood pressure is a more accurate marker of target organ damage.[12] One recently published study reported that central pulse pressure, indicative of changes in large conduit arteries, is an independent determinant of vascular remodeling in small retinal arterioles and concluded there was crosstalk between the microvascular and macrovascular changes attributable to hypertension.[13] Furthermore, the retina can be viewed as an extension of the brain. From a circulatory point of view, the brain is unique, because throughout systole and diastole it is perfused at high-volume flow[14] and because the cerebral circulation is auto-regulated.[15] In view of Ott's findings[13] and the high-volume flow to the brain,[14] we postulated that the diameter of the retinal microvessels might be tighter associated with central than peripheral blood pressure. We therefore investigated the relations of the diameters of the retinal arterioles and venules with central and peripheral blood pressure components.

Methods

Study population

Recruitment for the Flemish Study on Environment, Genes, and Health Outcomes (FLEMENGHO) started in 1985.[16] From August 1985 to November 1990, a random sample of the households living in a geographically defined area of Northern Belgium was investigated with the goal to recruit an equal number of participants in six subgroups stratified by sex and age (20–39, 40–59, and ≥60 years). All household members aged 20 years or older were invited, if the quota of their sex-age group had not yet been satisfied. From June 1996 until January 2004 recruitment of families continued using the former participants (1985–1990) as index persons and also including teenagers.[16] The initial participation rate was 78.0%.

The participants were repeatedly followed up. From January 2008 to July 2012, we mailed invitation letters to 1181 former participants for a follow-up examination at our field center including imaging of the retinal microvessels and pulse wave analysis. However, 29 participants had died and 17 were bedridden or institutionalized. We obtained informed written consent from 854. The participation rate was therefore 75.2%. From our current analyses, we excluded 249 participants with retinal images of low quality and 87 without pulse wave analysis. In addition, we excluded 4 participants from analysis, because their retinal phenotypes were more than 3 SDs higher than the mean. Thus, the number of participants analyzed totaled 514. FLEMENGHO was conducted according to the principles outlined in the Helsinki Declaration for Investigation of Human Participants.[17] The Ethics Committee of the Medical Faculty of the University of Leuven approved the study.

Hemodynamic measurements

Subjects had to refrain from smoking, heavy exercise, and drinking alcohol or caffeinated beverages for at least 3 h prior to the examination. After subjects had rested in the supine position for at least 15 min, trained observers ($n = 4$) measured blood pressure and subsequently did the arterial measurements. The observers performed two consecutive brachial blood pressure readings to the nearest 2 mmHg at the subjects' right arm by auscultation of the Korotkoff sounds, using a standard mercury sphygmomanometer (Riester GmbH, Jungingen, Germany), according to current European guidelines.[18] The two readings were averaged for analysis. Pulse pressure was systolic minus diastolic blood pressure. Mean arterial pressure was diastolic pressure plus one third of pulse pressure. Hypertension was a brachial blood pressure of at least 140 mmHg systolic or 90 mmHg diastolic or use of antihypertensive drugs.

During an 8-s period, the observers recorded the radial arterial waveform at the dominant arm by applanation tonometry. They used a high-fidelity SPC-301 micromanometer (Millar Instruments, Inc., Houston, TX) interfaced with a laptop computer running the SphygmoCor software (AtCor Medical Pty. Ltd., West Ryde, New South Wales, Australia), version 8.2. Recordings were discarded if systolic or diastolic variability of consecutive waveforms