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Research Article

Retinal arteriole-to-venule ratio changes and target organ disease evolution in newly diagnosed hypertensive patients at 1-year follow-up

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Abstract

There is no agreement on the systematic exploration of the fundus oculi (FO) in hypertensive patients, and it is unknown whether the evolution of retinal microcirculatory alterations has prognostic value or not. The aim of this study was to investigate whether the evolution of the arteriole-to-venule ratio (AVR) in newly-diagnosed hypertensive patients is associated with better or worse evolution of target organ damage (TOD) during 1 year. A cohort of 133 patients with newly-diagnosed untreated hypertension was followed for 1 year. At baseline and follow-up, all patients underwent a physical examination, self-blood pressure measurement, ambulatory blood pressure monitoring, blood and urine analysis, electrocardiogram, and retinography. The endpoint was the favourable evolution of TOD and the total amount of TOD, according to the baseline AVR and the baseline and final difference of the AVR. A total of 133 patients were analyzed (mean age, 57 ± 10.7 years; 59% men). No differences were found in the decrease in blood pressure or antihypertensive treatment between quartiles of baseline AVR or baseline-final AVR difference. Patients with a difference between baseline and final AVR in the highest quartile (>0.0817) had a favorable evolution of left ventricular hypertrophy (odds ratio, 14.9; 95% confidence interval, 1.08–206.8) and the amount of TOD (odds ratio, 2.22; 95% confidence interval, 1.03–6.05). No favorable evolution was found of glomerular filtration rate. There is an association between the evolution of the AVR and the favorable evolution of TOD. Patients with greater increase of AVR have significantly better evolution of left ventricular hypertrophy and amount of TOD. J Am Soc Hypertens 2014;8(2):83–93.

Keywords: Retinography; evolution of target organ damage; subclinical cardiovascular disease; left ventricular hypertrophy.

Introduction

Although clinical and epidemiological studies during the past half century[1,2] established the prognostic value of lesions of the fundus oculi (FO) in hypertensive patients, a discrepancy persists about their utility in routine practice in the initial examination of hypertensive patients.[3–5] Advanced lesions of the FO (exudates, hemorrhages, microaneurysms, and/or papilloedema) are considered as a vascular disease of the retina when it comes to risk-stratifying hypertensive patients.[6,7] However, injuries to

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the vessels of the retina (alteration of the arteriole-to-venule ratio [AVR], spasms of the arterioles, and arteriovenous crossings) are still a matter of debate due to highly variable inter- and intra-observer variabilities (20% to 42% and 10% to 33%, respectively).[8] Besides, reported prevalence of these lesions ranges between 7% and 80%.[4,9] Finally, a number of studies have found no relationship between initial lesions of the ocular fundus and blood pressure readings, or the presence of other manifestations of subclinical vascular disease.[3,10,11]

Retinography has attracted interest in the study of the FO.[12] This technique allows the calculation of various parameters of retinal vessels using automatic or semiautomatic applications. The most widely used parameter is the AVR.[13] The AVR has shown an association with metabolic syndrome,[14] with cerebral white matter lesions,[15,16] with cognitive disorder,[17] and with carotid stiffness.[18] It has also been associated with the future development of hypertension[19] or progression to more severe forms of hypertension,[20] diabetes mellitus,[21] heart failure,[22] and renal disease progression.[23] Finally, the AVR has shown an association with cardiovascular morbidity and mortality,[24–26] especially with stroke.[27,28]

There are no studies showing that regression of initial vascular lesions of the retina is associated with a better cardiovascular prognosis. Thus, the main objective of this study is to determine if the evolution of AVR in newly diagnosed hypertensive patients is associated with a better outcome of target organ lesions after 1 year.

Methods

Study Population

The VAMPAHICA study (acronym in Spanish for assessment of the self-monitoring of blood pressure in the diagnosis of isolated clinical hypertension) has been previously described.[29] In brief, this was a multicenter prospective study, involving 14 primary care centers in the Healthcare Region of Girona (Catalonia, Spain). All patients in this study were untreated hypertensive patients who had been recently diagnosed, and were recruited from 2003 to 2006.

Study Design

Patients who met the following criteria were included in the VAMPAHICA Study: a) aged 15 to 75 years; b) hypertension, defined as the average of two blood pressure (BP) readings, separated by 2 minutes, taken over three different days, with results of $\geq$140 and/or $\geq$90 mm Hg; c) recently diagnosed hypertensive patients who never received any treatment for hypertension; d) patients who provided corrected BP self-measurement and ambulatory BP monitoring. Exclusion criteria were the following: obvious inability, in the health professional's opinion, to perform BP self-measurements; diabetes mellitus; secondary hypertension; previous cardiovascular disease; renal insufficiency (serum creatinine $>$2 mg/dL); liver insufficiency; alcoholism or severe psychiatric disease; endocrine or severe haematological disease, or other severe diseases or limitations, which, in the physician's opinion, were a reason for exclusion. Diabetic patients were excluded to avoid confusing diabetic lesions with hypertensive lesions in the examination of the FO. Only those VAMPAHICA patients who fulfilled inclusion and exclusion criteria, and who underwent at least two retinographies of the eye fundus were included in this study.

All patients signed the informed consent, and the study protocol was approved by the Committee for Ethics and Clinic Research at the Health Care Institute (IAS).

Determination of BP and Control of Hypertension

Determination of Clinic BP

Hypertension was diagnosed based on measurements taken by the nurses with an armband adapted to the circumference of each patient's arm and following the standard conditions recommended by international organizations.[7]

BP Self-measurement Procedure

Each participant was instructed by a trained nurse, and performed the process twice in her presence to confirm that the readings were correct. Patients were provided with written instructions too. All the measurements were taken using OMRON 705 CP and OMRON 705 IT monitors (HEM 759 E2 and HEM 759 E; Tokyo, Japan) with an armband adapted to each patient's arm. Two readings were performed for three consecutive working days, one in the morning before breakfast, and two more in the evening before dinner. First day's readings were discarded.

Ambulatory BP Monitoring Procedure

Twenty-four-hour ambulatory BP monitoring was conducted 2 to 3 weeks after BP self-monitoring. The researcher performing ambulatory BP readings was not aware of the patient's self-obtained results. The following validated automatic oscillometric monitors were used: SpaceLabs 90,207, Spacelabs 90,217 (SpaceLabs, Redmond, WA). The monitors were programmed to carry out readings on a weekday, every 20 minutes along the day period (8:00 am to 23:00 pm) and every 30 minutes during the sleep period (23:01 pm to 7:59 am).

Both BP self-measurement, and ambulatory BP monitoring were performed at baseline and after 1 year.