International Journal of Cardiology 172 (2014) 59–63

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Leukoaraiosis and ambulatory blood pressure load in a healthy elderly cohort study: The PROOF study

John Avet [a,b], Vincent Pichot [c,d], Jean-Claude Barthélémy [c,d], Bernard Laurent [e,f], Arnauld Garcin [c,d], Frédéric Roche [c,d], Sébastien Celle [c,d,*]

[a] Service de radiologie, CHU Nord, 42055 Saint-Étienne, France
[b] Service de médecine nucléaire, CHU Nord, 42055 Saint-Étienne, France
[c] Service de Physiologie Clinique et de l'Exercice, Pôle NOL, CHU Nord, 42055 Saint-Étienne, France
[d] EA 4607 SNA-EPIS, Faculté de Médecine Jacques Lisfranc, Université Jean Monnet, PRES Université de Lyon42023 Saint-Étienne, France
[e] Service de neurologie, Pôle NOL, Université Jean Monnet, CHU Nord, 42055 Saint-Étienne, France
[f] Inserm U1028, Central Integration of Pain Lab, Université Claude Bernard Lyon 1, France

ARTICLE INFO

Article history:
Received 29 July 2013
Received in revised form 11 October 2013
Accepted 18 November 2013
Available online 23 November 2013

Keywords:
Hypertension
Leukoaraiosis
Aging

ABSTRACT

Background: Old age and hypertension are consistently reported to be the main risk factors of leukoaraiosis. The association between white matter lesions (WMLs) and other cardiovascular risk factors (CVRF) remains controversial. We evaluated the association between CVRF and WMLs in a cohort study and determined the blood pressure variables that could predict WML severity.
Methods: 830 subjects (65 +/− 1 years of age, 60% women) from the PROOF study, with a reliable ABPM and brain MRI, were included. The exclusion criteria included prior myocardial infarction, stroke, heart failure, atrial fibrillation, type 1 diabetes mellitus, and pacing. White matter changes on MRI were defined as hyperintensities >5 mm on FLAIR images. We used the total degree of WML (range: 0–30) by adding the region-specific scores of both hemispheres.
Results: Linear regression analyses demonstrated a significant relationship between total leukoaraiosis score and 24 h systolic blood pressure (SBP), 24 h diastolic BP, daytime SBP and DBP and nighttime SBP. No significant relationship was found between leukoaraiosis score and clinical SBP, clinical DBP, or nocturnal DIP. There was also no significant relationship between leukoaraiosis and other recognized cardiovascular risk factors. Based on a ROC curve analysis, we identified the optimal threshold separating high-risk WML patients for a mean 24 h SBP above 123 mm Hg ($p < 0.05$).
Conclusions: Even moderate increases in 24 h SBP promote arteriolar fragility of the cerebral white matter in a population aged 65. The prognostic implications of such abnormalities in asymptomatic and moderate cardiovascular risk populations remain to be evaluated.

© 2013 Published by Elsevier Ireland Ltd.

1. Introduction

White-matter lesions (WMLs) are frequently observed on cerebral magnetic resonance imaging (MRI) of elderly patients, even when they have no apparent neurological symptoms [1], and are an important prognostic factor for stroke [2], cognitive impairment, dementia [3,4], and premature death. WMLs are associated with degenerative changes in brain arterioles that are related to atherosclerosis. This suggests that cerebral arteriosclerosis of the penetrating vessels is a major factor in the pathogenesis of ischemic WMLs [5]. Old age and hypertension are consistently reported to be the main risk factors [6–8] for these lesions. Both average systolic blood pressure (BP) and the variability of systolic blood pressure have been linked to the presence of WMLs [9], although the results vary somewhat across published studies [10,11]. Twenty-four-hour ambulatory blood pressure monitoring (ABPM) has become an important tool that is used to improve the diagnosis and management of hypertension [12]. It is known that ABPM more strongly correlates with hypertension-related organ damage and cardiovascular events than do office blood pressure measurements [13]. The association between WMLs and other cardiovascular risk factors, such as type 2 diabetes, dyslipidemia or metabolic syndrome, remains controversial [14,15]. To our knowledge, no prospective study has examined the relationship between tobacco use, dyslipidemia, metabolic syndrome and WMLs in the elderly.

The aim of this study was to evaluate the associations between cardiovascular risk factors and WMLs in an elderly French cohort (i.e., the

* Corresponding author at: Service de physiologie clinique, Niveau 6, CHU de Saint-Étienne, 42055 Saint-Étienne, France. Tel.: +33 4 77 82 83 00; fax: +33 4 77 82 84 47.
E-mail address: sebastien.celle@univ-st-etienne.fr (S. Celle).

0167-5273/$ – see front matter © 2013 Published by Elsevier Ireland Ltd.
http://dx.doi.org/10.1016/j.ijcard.2013.11.052

PROOF study cohort) in subjects free of patent cerebrovascular disease and to determine the blood pressure parameters (measured using ABPM) that are most highly correlated with WMLs.

2. Methods

2.1. The PROOF study

The PROOF (PROgnostic indicator OF cardiovascular and cerebrovascular events) study is a large representative community survey of older adults who were recruited from the town of Saint-Étienne (France) and aged 65 years at the inclusion date [16]. The population of the study was selected among healthy volunteers who were expected to be at a low risk for cardiac or cerebrovascular events. The exclusion criteria were prior myocardial infarction, prior stroke, heart failure, atrial fibrillation, type 1 diabetes mellitus, cardiac pacing, and diseases limiting life expectancy to <5 years. The final population sample included 1011 subjects (60% of women). Detailed primary and secondary objectives of the PROOF study have been published elsewhere. In summary, the PROOF study was conducted to assess the role of decline in autonomic nervous system activity as a risk factor for cardiovascular events or death due to any cause. Subject assessment included clinical evaluation at the hospital by a cardiologist, an analysis of cardiovascular risk factors, and a survey of the concomitant therapeutic drugs prescribed to these volunteers. Ambulatory blood pressure and ECG Holter monitoring was then performed on an outpatient basis. Lastly, a brain MRI was conducted in subjects for whom MRI was not contraindicated to ensure the absence of silent stroke. Of the 1011 subjects identified, 830 were included who completed reliable ABPMs and brain MRIs, which allowed for the presence of white matter lesions to be evaluated.

The PROOF study was approved by an ERB (CCPRB Rhône-Alpes Loire) and all subjects signed a written informed consent.

2.2. Brain MRI

The brain MRIs were obtained using a 1-Tesla clinical MR unit (Magnetom Harmony; Siemens) equipped with an 8-channel phased array coil. The scanning protocol included axial sections of T2-weighted conventional spin-echo (TE = 121 ms, TR = 6620 ms, FOV = 173 * 230 mm^2, matrix size 115 * 256) and fluid-attenuated inversion recovery (FLAIR) (TR = 9000 ms, TE = 104 ms, inversion time = 2200 ms, FOV = 173 * 230 mm^2, matrix size = 182 * 256) sequences. The slice orientation was the axial plane perpendicular to the posterior margin of the pons, and the slice thickness was 5 mm, with a 1 mm inter-slice gap.

Only the FLAIR images were used to rate WMLs in this study because this sequence suppresses the cerebrospinal fluid (CSF) signal and it is sensitive to visualizing hyperintensities. Each scan was screened for other confounding neurological disorders.

2.3. Assessment of WML

The degree of WMH severity was rated using the axial FLAIR images via the visual age related white matter changes scale (ARWMC) [17]. White matter changes were defined as ill-defined hyperintensities >5 mm on FLAIR images [18] and were rated as shown in Table 1.

Five different regions were rated in the right and left hemispheres separately: 1) the frontal area, which comprised the frontal lobe anterior to the central sulcus; 2) the parietooccipital area, which consisted of the parietal and occipital lobes together; 3) the temporal area, which included the temporal lobe (the border between the parietooccipital and temporal lobes was approximated as the line drawn from the posterior part of the Sylvian fissure to the trigone areas of the lateral ventricles); 4) the infratentorial area, which included the brain stem and cerebellum; and 5) the basal ganglia, which included the striatum, globus pallidus, thalamus, internal and external capsules, and insula. The total degree of WMH (range: 0–30) was calculated by adding the region-specific scores of both hemispheres. All of the visual ratings were centrally conducted by a single rater who was blinded to subjects' clinical information. We did not use semi-automated threshold methods to quantify WMLs.

Table 1
The ARWMC rating scale for MRI.

Score	Definition
White matter lesions	
0	No lesions
1	Focal lesions
2	Beginning confluence of lesions
3	Diffuse involvement of the entire region, with or without involvement of U fibers
Basal ganglia lesions	
0	No lesions
1	1 focal lesion > 5 mm
2	More than 1 focal lesion
3	Confluent lesions

White matter changes on MRI were defined as bright lesions >5 mm on FLAIR images.

2.4. Blood pressure measurements

Clinical blood pressure was defined as the mean of 2 consecutive blood pressure measurements obtained by a physician with a mercury sphygmomanometer after the patient had been lying down for 15 min.

Twenty-four-hour ambulatory BP monitoring was assessed using valid, non-invasive auscultatory methods (Diasys Integra, Novacor, Rueil-Malmaison, France) [19]. Measurements were taken on a weekday beginning in the early morning. Automatic measurements were taken every 15 min during daytime and every 30 min during the night from the non-dominant arm. Subjects were instructed to continue their daily activities and regular sleeping habits as normal.

Average values of clinical systolic blood pressure (SBP) and diastolic blood pressure (DBP), 24-hour SBP and DBP, awake SBP and DBP, and sleep SBP and DBP were obtained for all of the subjects. Moreover, we calculated systolic and diastolic Dip as Dip = (1 − [-sleep BP / awake BP]), pulse pressure (PP) as PP = 24-hour SBP − 24-hour DBP, and mean arterial BP (MAP) as MAP = (24-hour SBP + [2 × 24-hour DBP]) / 3.

Hypertension was defined as either being treated (with at least one medication), having a mean DBP > 85 mm Hg and/or mean SBP > 130 mm Hg. An awake SBP > 135 mm Hg and a 24 h SBP > 130 mm Hg were defined as two markers of elevated BP on ABPM.

2.5. Cardiovascular risk factors

Risk factors other than blood pressure were evaluated in the PROOF study including the following: biological measures (fasting blood glucose, total cholesterol, HDL and LDL cholesterol, and triglyceride levels) as well as clinical anthropometric measurements (body mass index (BMI), waist circumference (WC), and tobacco smoking). In this study, the following thresholds were used: WC >102 cm for men and >88 cm for women, fasting plasma glucose concentration >6.1 mmol/L or use of hypoglycemic medication, plasma HDL-cholesterol concentration <1.03 mmol/L for men and <1.29 mmol/L for women, and plasma triglycerides concentration >1.69 mmol/L [20].

2.6. Statistical methods

We performed statistical analyses using a linear regression model with each blood pressure measurement (clinical SBP and DBP, ambulatory SBP and DBP, PP, MAP) and common risk factors (age, tobacco use, waist circumference, BMI, fasting blood glucose level, total cholesterol, HDL-cholesterol, LDL-cholesterol, LDL/HDL cholesterol and triglycerides) as dependent variables and leukoaraiosis, gender and hypertension status as independent variables. A linear regression was then performed using the subjects who were free of antihypertensive medications; each blood pressure measurement was used as a dependent variable, and gender and leukoaraiosis were used as independent variables.

Common metabolic syndrome thresholds were used to separate our population into two groups: those with metabolic syndrome and those without metabolic syndrome. Student's *t*-test was applied to compare mean leukoaraiosis scores/severity between these two groups.

Using ROC curves, we also attempted to define a blood pressure threshold to discriminate between individuals with low levels of leukoaraiosis and individuals with high levels of leukoaraiosis; these groups were defined using the median leukoaraiosis score observed in the entire sample.

3. Results

For a total of 830 subjects, biological measurements, ambulatory blood pressure recordings and validated brain MRIs were obtained. Table 2 presents the characteristics of the population of study and Table 3 summarizes regional leukoaraiosis scores.

Evaluating the two subgroups in relation to the known thresholds for fasting blood glucose, WC, BMI, HDL cholesterol, HDL/LDL or triglycerides or blood pressure measurements, the leukoaraiosis score was determined to be significantly different only between subjects with elevated blood pressures or with treatment and normotensive subjects. As expected, leukoaraiosis severity was found higher in subjects under anti-hypertensive medication ($p = 0.015$).

Linear regression analyses revealed a significant relationship between total leukoaraiosis scores and 24 h SBP and 24 h DBP, daytime SBP and DBP and nighttime SBP. No significant relationship was found between leukoaraiosis scores and clinical SBP, clinical DBP or systolic and diastolic DIP. The relationship between total leukoaraiosis and nighttime DBP approached significance but was non-significant. The total leukoaraiosis score was also significantly associated with PP and MAP. These results are summarized in Table 4.

In untreated and supposedly normotensive subjects, the total leukoaraiosis score was significantly associated with all of the BP measurements, except for clinical SBP and DBP, and systolic and diastolic

Download English Version:

https://daneshyari.com/en/article/5972382

Download Persian Version:

https://daneshyari.com/article/5972382

Daneshyari.com