Nutrition, Metabolism & Cardiovascular Diseases (2015) 25, 160–166

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

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

Renal haemodynamics and severity of carotid atherosclerosis in hypertensive patients with and without impaired renal function

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Received 8 August 2014; received in revised form 29 September 2014; accepted 14 October 2014
Available online 24 October 2014

KEYWORDS
Renal resistive index;
Carotid atherosclerosis;
Hypertension;
Chronic kidney disease

Abstract *Background and aim:* Renal resistance index (RRI), assessed by Duplex-Doppler sonography, has been classically considered as a mere expression of intrarenal vascular resistance. Recent studies, however, have showed that RRI is also influenced by upstream factors, especially arterial compliance, confirming its possible role as a marker of systemic vascular alterations.

Several studies have shown that carotid intima-media thickness (cIMT) and carotid plaques (cP), assessed by ultrasonography, are documented markers of subclinical organ damage as well as expression of progressive atherosclerotic disease, and that they get worse with the progressive deterioration of renal function.

The study was aimed to evaluate the relationship between RRI and severity of carotid atherosclerosis in hypertensive subjects with and without impaired renal function.

Methods and results: The study population, including 263 hypertensive patients (30–70 years), was split into 3 groups based on cIMT and presence of cP (cIMT $\leq$ 0.9 mm and no cP; cIMT $>$ 0.9 mm and no cP; cP). All patients were also divided into 2 subgroups (normal renal function; CKD stage I–IV).

A stepwise increase in RRI corresponding to the groups of progressive severity of carotid atherosclerosis was observed (respectively 0.61 $\pm$ 0.07, 0.65 $\pm$ 0.06, 0.68 $\pm$ 0.06; $p < 0.001$). A strong positive correlation was observed between RRI and cIMT in the whole population ($r = 0.43$; $p < 0.001$) and in the subgroups with ($r = 0.42$; $p < 0.001$) and without ($r = 0.39$; $p < 0.001$) CKD. These associations remained statistically significant even after adjustment for various confounding factors.

Conclusion: Showing a close association between RRI and severity of carotid atherosclerosis, our results strengthen the concept that RRI is a marker of systemic vascular changes.

Background

The renal resistance index (RRI), measured by Duplex-Doppler ultrasonography, is the most widely used parameter to assess renal haemodynamics noninvasively [1].

RRI was classically considered as a mere expression of vascular resistance involving the local intrarenal district. Thus, it was used as a diagnostic tool and as a prognostic factor in numerous pathological conditions characterized by impaired intrarenal impedance, especially renovascular disease [2] and chronic kidney disease [3].

More recent data, however, have shown that RRI may be also influenced by upstream vascular factors, first of all arterial stiffness [4], and indeed these factors appear to play a more important role than intrarenal resistance in

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http://dx.doi.org/10.1016/j.numecd.2014.10.008
0939-4753/

determining RRI [5]. Moreover, this haemodynamic index has been associated with endothelial dysfunction [6], with subclinical organ damage [7,8] and with unfavorable cardiovascular outcomes [9], thus suggesting its potential role as a marker of systemic morphofunctional arterial impairment, particularly in hypertensive subjects with or without normal renal function [7,10].

Different markers are used to assess subclinical vascular damage. Among all, carotid intima-media thickness (cIMT) and carotid plaques (cP), both assessed by ultrasonography, represent expression of progressive atherosclerotic carotid disease, which has already shown a strong relationship with coronary and systemic atherosclerosis [11]. Moreover, several studies demonstrated that cIMT and cP were associated with other early markers of target organ damage, such as arterial stiffness [12] or renal dysfunction [13], and with cardiovascular events [11,14,15].

Although there are many studies that correlate cIMT and renal haemodynamics in hypertensive patients [7,8], few data exist about the relationship between RRI and degree of early carotid atherosclerotic damage.

The aim of our study was to evaluate the relationship between RRI and severity of carotid atherosclerosis, assessed by both cIMT or cP, in hypertensive subjects with and without impaired renal function.

Methods

Subjects

The population of this cross-sectional study was selected from 356 Caucasian hypertensive patients consecutively attending our unit of Nephrology and Hypertension. Most of them had been referred to our institution by their general practitioners for specialist advice.

The exclusion criteria were:

- Age lower than 30 years and greater than 70 years.
- Renovascular, malignant or endocrine hypertension.
- Severe obesity, defined as a body mass index (BMI) $\geq$ 40 kg/m^2.
- End-stage renal disease [stage V of KDIGO (Kidney Disease Improving Global Outcomes) classification [16]].
- Rapid deterioration of renal function (decrease in eGFR >25% within 7 days).
- Kidney allograft.
- Hydronephrosis of grade 2 or higher.
- Patients with significant difference in size or morphology between kidneys.
- Permanent atrial fibrillation.
- Heart rate >100 bpm or <50 bpm.
- Heart failure.
- Moderate to severe aortic/mitral valve disease.
- Major non-cardiovascular diseases.
- Low quality renal sonographic recordings.

Written informed consent was obtained from each subject. The study protocol, that conforms to the ethical guidelines of the declaration of Helsinki, was approved by the local review board.

In all subjects, careful clinical history and physical examination were performed. Body weight and height were measured by a nurse and clinic blood pressure was recorded by a doctor, following the recommendations of the 2013 European Society of Hypertension/European Society of Cardiology guidelines [17].

Clinic blood pressure was considered as the mean of three consecutive measurements obtained, at 2 min intervals, by an electronic oscillometric validated device (Microlife Watch BP Office) [18], after 5 min of rest in sitting position. Furthermore, a 24 h ambulatory blood pressure monitoring (ABPM) was carried out through a portable, non-invasive SpaceLabs 90207 recorder (Redmond, Washington, USA).

Persons who reported smoking cigarettes regularly during the past year were considered current smokers.

Fasting blood samples were drawn to perform routine blood chemistry and a 24 h urine sample was collected to evaluate the levels of albumin excretion. Definition and classification of chronic renal disease followed the K/DIGO guidelines [16]. GFR was estimated by using CKD-EPI (Chronic Kidney Disease – Epidemiology Collaboration) equation [19].

Moreover, a B-mode and Duplex-Doppler ultrasonographic examination of both intrarenal and carotid vasculature was performed by 2 different well-trained operators (MM and CG), unaware of clinical data of patients. Each operator was also not aware of the results obtained by the other one.

Renal ultrasonography

The intrarenal colour duplex ultrasonography was performed through a GE Logiq P5 PRO instrument (General Electric Company, Milan, Italy), with a 4 MHz transducer operating at 2.5 MHz for Doppler analysis. The Doppler signal was obtained from the interlobar arteries by placing the sample volume at the level of the cortico-medullary junction. Peak systolic velocity (PSV) and telediastolic velocity (TDV) were measured, and so RRI was calculated by the formula: $RRI = (PSV - TDV)/PSV$. The values were computed as the average of six measurements (three from each kidney). The Doppler angle chosen was less than 60°, and special care was taken not to compress the kidney and not to have the patient perform a Valsalva manoeuvre, because both can increase the RRI [4].

Carotid ultrasonography

The carotid ultrasonographic investigation was performed with a GE Logiq P5 PRO device (General Electric Company, Milan, Italy) through a 10 MHz linear-array transducer for the measurements, operating at 5 MHz for Doppler analysis.

The examination was obtained with the subject lying down, with the head extended and slightly turned opposite to the carotid being examined, following the