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Choroidal thickness is associated with renal hemodynamics in essential hypertension

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Abstract

The choroid is the most vascularized structure of the eye and plays a central role in the development of the retinal vascular changes that occur in arterial hypertension. Changes of choroidal thickness (ChT) assessed by optical coherence tomography (OCT) technology could reflect the vascular complications of hypertension. Also, intrarenal hemodynamic damage, associated with endothelial dysfunction, demonstrated to be a good indicator of systemic morphofunctional arterial impairment. The aim of this study is to assess the relationship between ChT and renal hemodynamics in subjects with essential hypertension. Routine laboratory tests, clinical history, and physical examination, including blood pressure assessment, were performed in 90 subjects with essential hypertension. All patients underwent Doppler ultrasonographic evaluation of intra-renal hemodynamics and OCT imaging to assess ChT. When subjects were divided in two groups based on renal resistive index (RRI), group I (RRI ≥ 75% percentile) showed significantly lower values of ChT than group II (RRI < 75% percentile) ($P < .001$). When divided in two groups based on the ChT median values, patients with lower ChT had significantly higher RRI values than those with ChT above the median values ($P < .05$). In multivariate model including age, eGFR, and other variables as confounding factors, RRI ≥ 75% was independently associated with ChT. ChT was significantly correlated with renal resistive index in subjects with essential hypertension, confirmed in multivariate analyses. This result could be referred to changes in vascular elastic properties that occur in retinal and intrarenal vascular system probably due to oxidative stress and endothelial dysfunction commonly found in early complications of hypertension.

1 | INTRODUCTION

Arterial hypertension is an independent risk factor for cardiovascular mortality as well as for the development and progression of chronic kidney disease (CKD).[1] The unfavorable long-term effects of hypertension are associated with structural and functional impairment of blood vessels. Adaptive changes occur in both small arteries and microcirculation and could predict the onset of target organ damage and hypertension complications.[2,3]

The retina has been traditionally considered the most easily accessible window to study systemic microcirculation,[4] thus allowing direct observation in vivo of hypertension microvascular

damage[5] that has proved to be predictive of cardiovascular and renal events.[2,6]

However, the choroid (and not the retina) is the most vascularized structure of the eye as well as the tissue with the highest vascular density in the body[11]: It provides vascular supply to the contiguous retina, and it plays a central role in the development of retinal vascular changes.[7,8] It is therefore reasonable that morphological alterations of the choroid could represent the local epiphenomenon of a systemic microvascular injury not less than the retinal ones, and the evidence that choroid may be directly damaged by an increase in blood pressure seems to confirm this hypothesis.[9]

In recent years, the advances in optical coherence tomography (OCT) technology have allowed to study choroidal vasculature and structure in a detailed and reproducible way, by overcoming technical limitations related to previous investigation tools.[10] In particular, the assessment of choroidal thickness (ChT) has gradually gained a leading role in the study of microcirculation because it is globally considered as morphological surrogate and structural expression of the choroidal vascular system.[11] Changes in ChT have been therefore observed in subjects with diabetes, coronary artery disease, and in other conditions likewise characterized by systemic microvascular damage, including chronic kidney disease and hypertension.[5,9,12-14] However, some evidence does not confirm the relationship between ChT and blood pressure, and conflicting data are observed in different studies.[15,16] It is conceivable that ChT could early reflect the vascular consequences of hypertension rather than hypertension itself, so explaining the heterogeneity of literature data.

Since the eye and the kidney have common developmental, structural, and pathogenic pathways,[17] changes in choroidal circulation could therefore relate with intrarenal hemodynamic damage, which has been associated with endothelial dysfunction,[18] subclinical organ damage,[19,20] and unfavorable cardiovascular outcomes,[21] and which appears a good indicator of systemic morphofunctional arterial impairment, particularly in hypertensive subjects with or without normal renal function.[22,23]

The aim of this study is to assess the relationship between ChT and renal hemodynamics, noninvasively assessed by duplex-Doppler ultrasonography, in subjects with essential hypertension.

2 | MATERIALS AND METHODS

2.1 | Study population

The population of this cross-sectional study was selected from Caucasian subjects with essential hypertension consecutively attending our Unit of Nephrology and Hypertension—European Society of Hypertension Excellence Center of the University of Palermo between May 2016 and May 2017.

The exclusion criteria were as follows:

- Age <20 and >70 years;
- Ocular diseases and/or a history of ophthalmic surgery;
- Renovascular, malignant, endocrine hypertension, or hypertension associated with obstructive sleep apnea syndrome;
- Hereditary or congenital renal diseases, nephritic diseases, and known proteinuria/hematuria;
- Estimated GFR (eGFR) <15 mL/min/1.73 m^2 or renal replacement therapy (transplanted or dialyzed patients);
- Rapid deterioration of renal function, defined as a reduction in eGFR >25% or an increased serum creatinine >1.5 times baseline[24];
- Low-quality renal sonographic recordings or abnormal renal morphology, as described elsewhere[25];
- History of diabetes or fasting glycemia >126 mg/dL;
- History or clinical signs of heart failure (NYHA class II-IV), coronary artery disease, or cerebrovascular disease;
- Major noncardiovascular diseases (liver cirrhosis, chronic obstructive lung disease, and anamnestic presence of neoplasms).

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

2.2 | Clinical and laboratory evaluation

Careful clinical history and physical examination were performed in all subjects. Body weight, height, and waist circumference were measured by a nurse. Subjects who reported smoking cigarettes regularly during the past year were considered current smokers. Clinic blood pressure (BP) was recorded by a doctor, following the recommendations of the 2018 European Society of Hypertension/European Society of Cardiology guidelines.[26] It was considered as the mean of three consecutive measurements obtained at 2-minutes intervals by an electronic oscillometric validated device (WatchBP Office, Microlife AG) 20 after 5 minutes of rest in a sitting position. Hypertension was defined as a BP ≥140/90 mm Hg or treatment with antihypertensive drugs,[26] and secondary forms of hypertension were excluded.

Routine biochemical parameter determination was performed in all patients with standard techniques using an autoanalyzer (Boehringer Mannheim for Hitachi system 911). Low-density lipoprotein cholesterol was calculated by the Friedewald formula. Estimated GFR (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Equation.[27]

2.3 | Ultrasonographic evaluation

The intrarenal duplex ultrasonography was performed in all patients by a single well-trained operator, unaware of the patient's clinical data, through a GE Logiq P5-PRO instrument (General Electric Company), with a 4 MHz transducer operating at 2.5 MHz for Doppler analysis. All measurements were obtained in the supine position, and the Doppler signal was obtained from the interlobar

arteries by placing the sample volume at the level of the corticomedullary junction. Renal resistive index (RRI) was calculated by the formula: RRI = (Peak systolic velocity − telediastolic velocity)/peak systolic velocity. 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 maneuver, because both can increase the RRI.

2.4 | Ophthalmic evaluation

All of the patients underwent complete eye examinations, including best-corrected visual acuity with Early Treatment Diabetic Retinopathy Study (ETDRS) charts, intraocular pressure measurements, and anterior segment and dilated fundus evaluations. A single examiner, not aware of the clinical and biohumoral data of the patient, established the presence and level of hypertensive retinopathy, using the Keith, Wagener, and Barker classification.[28] The retino-choroidal district was evaluated morphologically by accurate Swept-Source OCT (SS-OCT) (DRI Triton, Topcon Inc), always in the morning during the same temporal interval (10-12 AM). All of the scans were performed by a single operator following a standardized protocol for all of the scans, and poor-quality scans were rejected or repeated. The scans were then read and analyzed by two specialized ophthalmologists. The right eye was examined first, and because no significant differences were noted between the two eyes, only one eye of each subject was randomly selected for analysis using a random number generator. If the image quality of the selected eye was deemed insufficient, the contralateral eye was chosen for analyses.

The retinal thickness (from the inner limiting membrane to the inner surface of the retinal pigment epithelium, RPE) and ChT (from the outer surface of the RPE to the choroidal-scleral interface, CSI) were automatically calculated by the SS-OCT mapping software. OCT measurements were performed according to the ETDRS protocol.[29] The ETDRS map divides the macula into nine subfields: The circular grid is centered over the fovea and consists of three concentric rings 1, 3, and 6 mm in diameter, respectively. The inner and outer rings are further divided into quadrants: temporal, nasal, superior, and inferior (Figure 1A).

Measurements are displayed for each of the nine regions of the ETDRS grid for both the retina and the choroid. We calculated the central ring (ChT-cr) and the average of the individual values of the four quadrants separately for the inner and outer rings: the average inner ring (ChT-air) and the average outer ring (ChT-aor). The average of all nine regions (overall ring) of the ETRDS grid (including the inner, the outer, and the central rings) was also calculated (ChT-or). A single observer measured the ChT perpendicularly from the outer portion of the hyperreflective line, corresponding to the RPE, to the CSI, as previously described (Figure 1B).

2.5 | Statistical analysis

The final analysis involved 90 hypertensive patients. Statistical analysis was initially performed in the whole study population, and it was subsequently carried out in the population divided based on RRI values ≥ or <75% percentile (cutoff value: 0.663; respectively n = 22 and n = 68). The statistical analysis was also performed in subjects with choroidal thickness (central ring, average inner ring, average outer ring, overall ring) above and below the median value.

Normal distribution of the continuous variables was assessed using the Kolmogorov-Smirnov test. Continuous variables were given as mean ± standard deviation. Triglycerides (expressed as median and interquartile range because of its skewed distribution) were log-transformed to better satisfy distributional assumptions before parametric tests were used. Categorical variables were expressed as percentage values. Student's *t* test for independent samples was used to compare continuous variables between groups. For the categorical variables, comparisons were performed using the χ^2 test, with the Monte Carlo method for computation of exact two-tailed α-values. Simple regression analyses and Pearson's correlation coefficients were used to test the relationships between choroidal thickness measurements, RRI, and the other variables.

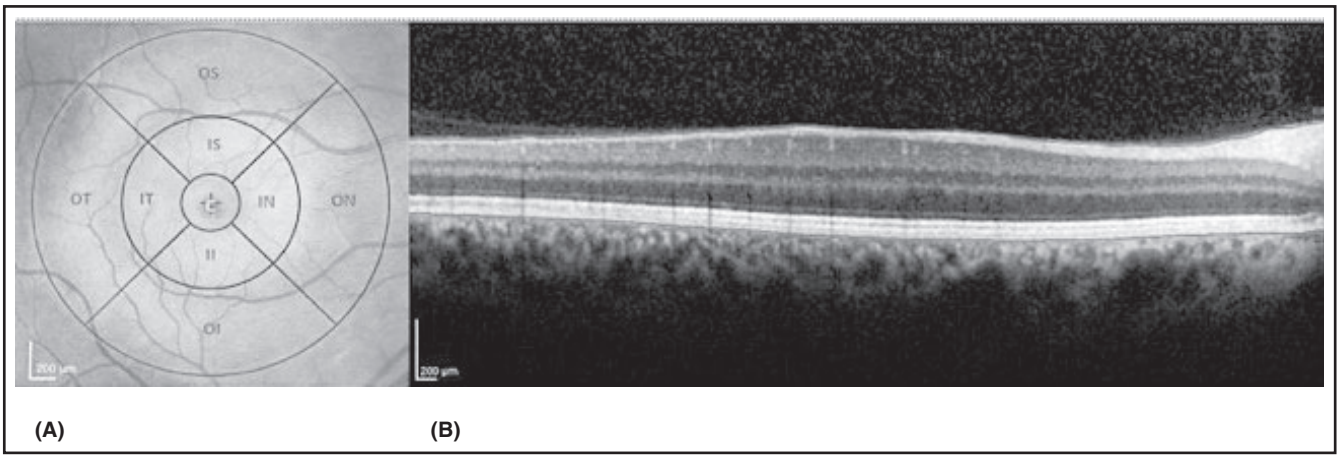

FIGURE 1 Choroidal and retinal structures shown in frontal (A) and transverse section (B)

The multivariate relationships between ChT measurements with other variables were tested by multiple linear regression models performed considering ChT-cr (or alternatively ChT-air, ChT-aor, or ChT-or) as outcome variable and including as covariates: age, sex (0 = females; 1 = males), eGFR, RRI (0 = <75% percentile; 1 = ≥75% percentile), BMI, LDL cholesterol, clinic mean BP, therapy with statins (0 = no treatment; 1 = treatment). In this analysis, a backward stepwise procedure was used, with α = .15 as the cutoff for the entry or removal of variables.

Collinearity was assessed by calculating the variance inflation factor (VIF): Variables with VIF ≥2 were excluded from the models. The null hypothesis was rejected with a two-tailed $P < .05$. The statistical analyses were performed using the IBM SPSS Statistics software package, version 23 for Macintosh (SPSS).

3 | RESULTS

Table 1 summarizes the characteristics of the overall study population (n = 90) and of the two groups divided based on renal resistive index (cutoff: 75% percentile). Subject in group I (RRI ≥ 75% percentile) showed significantly lower values of ChTs than those in group II (RRI < 75% percentile) (all $P < .001$).

No differences in RRI or ChT values were observed between males and females. Patients with eGFR ≤ 60 mL/min/1.73 m^2 had significantly higher RRI values ($P < .001$) and lower ChT-cr, ChT-aor, and Cht-or (all $P < .010$) than subjects with normal renal function, and similar results were observed in smokers compared to nonsmokers (all $P \leq .010$) (see Table S1).

TABLE 1 Characteristics of the overall study population and of the two groups divided based on renal resistive index (cutoff: 75% percentile)

	Overall population (n = 90)	RRI-I (n = 68)	RRI-II (n = 22)	*P*-value
Age (y)	49 ± 12	46 ± 11	59 ± 13	<.001
Male gender, n (%)	64 (71.1)	51 (75.0)	13 (59.1)	*NS*
Smoke, n (%)	38 (42.2)	28 (41.2)	10 (45.6)	*NS*
BMI (Kg/m^2)	28.1 ± 4.7	27.8 ± 4.5	29.3 ± 4.9	*NS*
eGFR < 60 mL/min/1.73 m^2, n (%)	13 (14.4)	5 (7.4)	8 (36.4)	.002
Hypolipidemic therapy, n (%)	17 (18.9)	7 (10.3)	10 (45.5)	.001
Antihypertensive therapy, n (%)	70 (77.8)	51 (75.0)	19 (86.4)	*NS*
Clinic systolic BP (mm Hg)	136 ± 12	137 ± 13	135 ± 9	*NS*
Clinic diastolic BP (mm Hg)	85 ± 9	86 ± 9	82 ± 9	.035
Clinic pulse pressure (mm Hg)	51 ± 9	50 ± 9	53 ± 9	*NS*
Clinic mean BP (mm Hg)	102 ± 9	103 ± 10	99 ± 8	*NS*
Clinic heart rate (beats)	74 ± 11	74 ± 11	71 ± 11	*NS*
Biochemical parameters				
Serum glucose (mg/dL)	96.1 ± 14.9	94.5 ± 16.4	101.2 ± 13.2	*NS*
Serum uric acid (mg/dL)	6.27 ± 1.63	6.15 ± 1.68	6.66 ± 1.46	*NS*
Serum total cholesterol (mg/dL)	193 ± 29	197 ± 28	181 ± 29	.018
LDL-c (mg/dL)	121 ± 28	126 ± 27	107 ± 27	.006
HDL-c (mg/dL)	48 ± 11	48 ± 10	47 ± 12	*NS*
Serum triglycerides (mg/dL)	117 (86-150)	107 (78-140)	115 (88-164)	*NS*
Serum creatinine (mg/dL)	1.01 ± 0.25	0.99 ± 0.25	1.08 ± 0.23	*NS*
eGFR (mL/min/1.73 m^2)	84.1 ± 22.0	88.5 ± 20.3	70.4 ± 21.8	.001
Serum sodium (mEq/L)	140 ± 3	140 ± 3	141 ± 3	*NS*
Serum potassium (mEq/L)	4.26 ± 0.40	4.25 ± 0.40	4.30 ± 0.40	*NS*
Choroidal thickness				
Central ring (μm)	267.2 ± 81.2	286.6 ± 74.7	207.1 ± 71.9	<.001
Average inner ring (μm)	252.5 ± 68.1	268.3 ± 61.0	203.6 ± 66.7	<.001
Average outer ring (μm)	234.0 ± 63.3	247.9 ± 56.8	191.0 ± 64.3	<.001
Overall ring (μm)	250.8 ± 67.6	267.3 ± 59.7	199.9 ± 66.6	<.001
Ultrasonographic parameters				
RRI	0.62 ± 0.06	0.59 ± 0.05	0.70 ± 0.04	<.001

Abbreviations: BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; RRI, renal resistive index.

TABLE 2 RRI values (mean ± standard deviation) and RRI ≥ 75% percentile (percentage) in the population divided into 2 groups based on the ChT median values

	RRI	*P*-value	RRI ≥ 75% percentile (%)	*P*-value
ChT-cr				
≥268.0 (μm)	0.61 ± 0.05	.043	11.1%	.003
<268.0 (μm)	0.64 ± 0.07		37.8%	
ChT-air				
≥249.5 (μm)	0.60 ± 0.06	.012	13.3%	.013
<249.5 (μm)	0.64 ± 0.07		35.6%	
ChT-aor				
≥235.0 (μm)	0.60 ± 0.06	.010	13.3%	.013
<235.0 (μm)	0.64 ± 0.06		35.6%	
ChT-or				
≥252.9 (μm)	0.61 ± 0.05	.021	11.1%	.003
<252.9 (μm)	0.64 ± 0.07		37.8%	

Abbreviations: AIR, average inner ring; AOR, average outer ring; ChT, choroidal thickness; CR, central ring; OR, overall ring; RRI, renal resistive index.

When we divided the entire population in 2 groups based on the ChT median values, patients with lower ChTs had significantly higher RRI values than those with ChTs above the median values (all $P < .05$) (see Table 2).

The percentage of patients treated with cardiovascular drugs in the overall study population and in the two groups divided based on renal resistive index are showed in Table S2.

The univariate correlations of RRI and ChTs with other variables in the entire study population are shown in Table 3. Estimated GFR was associated with both RRI and ChT values in the entire population (all $P < .001$). RRI significantly correlated with all ChT measurements in all subjects (all $P < .001$) (Figure 1), without significant differences when we separately analyzed these relationships differently in women and men; similarly, no differences were found when we separately compared these relationships in the groups divided by smoking habit. The associations between the abovementioned variables held also after adjustment for eGFR ($r = .244$; $P = .021$).

When we performed multivariate analysis considering ChT-cr as outcome variable, RRI ≥ 75% was associated with choroidal thickness independently of other covariates included in the model (described in the statistical section), and similar results were observed when we

TABLE 3 Main correlations of choroidal and ultrasonographic parameters in the entire study population

	ChT-cr	ChT-air	ChT-aor	ChT-or	RRI
	r	*r*	*r*	*r*	*r*
Age	−.514***	−.550***	−.565***	−.562***	−.394***
BMI	$-.118^{NS}$	$-.172^{NS}$	$-.175^{NS}$	$-.149^{NS}$	$.135^{NS}$
Clinic systolic BP	$.195^{NS}$	$.186^{NS}$	.225*	$.188^{NS}$	$-.003^{NS}$
Clinic diastolic BP	.244*	−.292**	.267*	.244*	−.229*
Clinic pulse pressure	$.011^{NS}$	$-.050^{NS}$	$.027^{NS}$	$.002^{NS}$	.227*
Clinic mean BP	.246*	.273**	.274**	.243*	$-.152^{NS}$
Clinic heart rate	$.090^{NS}$	$.103^{NS}$	$.114^{NS}$	$.100^{NS}$	$-.131^{NS}$
Serum glucose	$-.185^{NS}$	−.263*	−.252*	−.242*	−.236*
Serum uric acid	$-.011^{NS}$	$-.051^{NS}$	$-.096^{NS}$	$-.074^{NS}$	$.162^{NS}$
Serum total cholesterol	$.166^{NS}$	$.160^{NS}$	$.206^{NS}$	$.187^{NS}$	−.221*
LDL-c	.26*	.227*	.286**	.269**	−.257*
HDL-c	$-.082^{NS}$	$-.038^{NS}$	$-.039^{NS}$	$-.034^{NS}$	$-.020^{NS}$
Serum triglycerides	$-.157^{NS}$	$-.121^{NS}$	$-.164^{NS}$	$-.173^{NS}$	$.094^{NS}$
Serum creatinine	$-.122^{NS}$	$-.075^{NS}$	$-.124^{NS}$	$-.181^{NS}$	$.167^{NS}$
eGFR	.361***	.331***	.366 ***	.408***	−.345***

Note: $^{NS}P > .05$.

Abbreviations: BMI, body mass index; BP, blood pressure; ChT-air, choroidal thickness-average inner ring; ChT-aor, choroidal thickness-average outer ring; ChT-cr, choroidal thickness-central ring; ChT-or, choroidal thickness-overall ring; eGFR, estimated glomerular filtration rate; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; RRI, renal resistive index.

*$P \leq .05$.

**$P \leq .01$.

***$P \leq .001$.

TABLE 4 Independent multivariate correlates of ChT-cr [A] and ChT-or [B] in the overall study population

Outcome variable: [A] ChT-cr	Regression coefficients: Standardized β	P
Model (R^2 = 0.314)		
Age (y)	−0.408	<.001
RRI ≥ 75% percentile	−0.247	.014
Outcome variable: [B] ChT-or	**Regression coefficients: Standardized β**	**P**
Model (R^2 = 0.359)		
Age (y)	−0.462	<.001
RRI ≥ 75% percentile	−0.231	.017

Note: The other variables included in the models are described in the text (statistical section).

Abbreviations: ChT-cr, Choroidal Thickness-central ring; ChT-or, Choroidal Thickness-overall ring; RRI, Renal Resistive Index.

further considered as outcome variable ChT-or (see Table 4), but not ChT-air or ChT-aor (*P* = .050 e *P* = .109).

4 | DISCUSSION

The choroid is a pure vascular structure, and changes in ChT represent proxy measures of impaired district blood flow, so reflecting a microvascular damage that might be the local expression of a more generalized vascular injury.

Hypertension might play a leading role in determining structural modification of choroidal layer, and it might be considered as a potential determinant of choroidal thickness, causing the so-called "hypertensive choroidopathy" as defined by Hayreh et al[30] In a population of 160 subjects (80 hypertensives and 80 healthy controls), Akay et al demonstrated that choroidal thickness decreased in patients with systemic arterial hypertension,[5] and overlapping findings were reported by Masís et al in a similar population, although these results could reflect only a between-group age difference.[31] However, several evidences did not seem to confirm a direct causal role of BP on ChT structural changes,

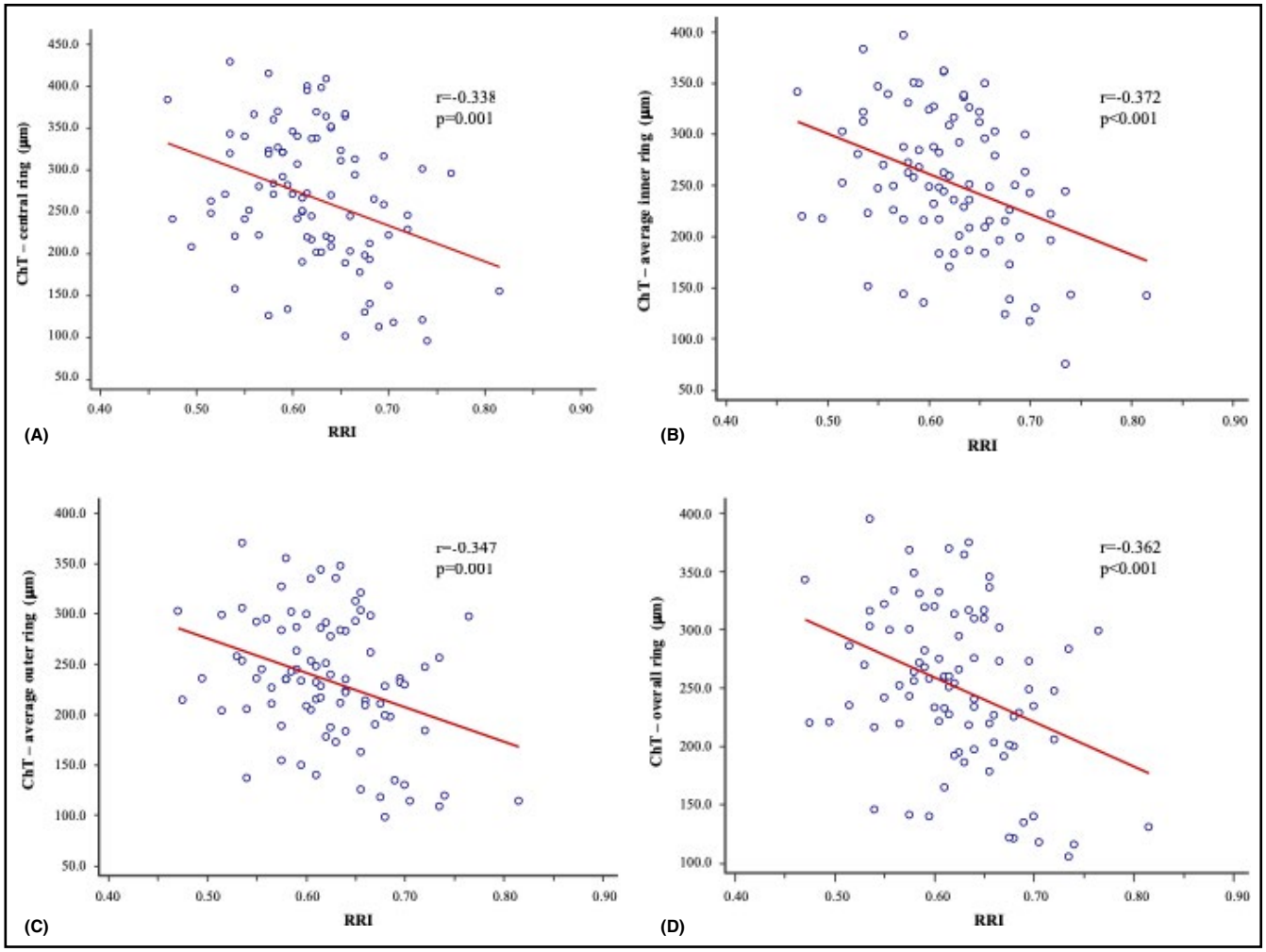

FIGURE 2 Univariate correlations between renal resistive index (RRI) and choroidal thickness (ChT) central ring (A), average inner ring (B), average outer ring (C), and overall ring (D) in the entire study population

and conflicting data are observed in different studies.[15,16] Gök et al did not observe significant differences in subfoveal ChT between 116 patients with arterial hypertension compared to 116 healthy controls,[15] and Ahn et al rather demonstrated significant increase in subfoveal ChT in subjects with severe hypertension and hypertensive retinopathy, possibly due to choroidal permeability changes with subsequent interstitial fluid accumulation in the choroid layer.[9] In line with abovementioned evidences, in our study we did not observe any independent relationship between ChT and clinic BP when we performed multivariate analyses: It is so conceivable that ChT could early reflect the vascular consequences of hypertension rather than the hypertension itself, and this could explain some inconsistencies and the heterogeneity of literature data.

Several studies have showed that impaired intrarenal hemodynamics was an expression of systemic vascular damage in hypertensive patients, and in recent years many authors highlighted that duplex-derived RRI was associated with hypertensive-related morphofunctional changes rather than with BP itself, similarly to our data observed in the present study.[19,23] Since the eye and the kidney share much of vascular structure and pathogenic pathways,[17] and according with the abovementioned speculation, we hypothesized that ChTs would be associated with intrarenal hemodynamic changes in hypertensive subjects. In the entire study population, all the ChT measurements were significantly correlated with RRI (see Figure 2), and these relationships hold out even after multivariate analyses including age, eGFR and other variables as confounding factors (Table 4).

No study currently exists that specifically analyzes the relationship between choroidal thinning and increased intrarenal resistance in hypertensive population; however, this link could have different possible explanations, and several pathophysiological mechanisms could be hypothesized.

Oxidative stress and endothelial dysfunction, both typical of the early stages of hypertension, have proven to play a key role in determining structural changes of choroidal layer, as previously demonstrated with regard to renal resistive index by Raff et al[18] In a population of 150 patients (50 with hypertension, 50 with CKD and 50 healthy controls), Balmforth et al observed that a thinner choroid was associated with increased circulating C-reactive protein, IL-6, asymmetric dimethylarginine, and endothelin-1[32]: Due to endothelial dysfunction, powerful vasoconstrictors could easily pass from the fenestrated choriocapillaris to the interstitial area, trigger severe vasoconstriction, and produce tissue ischemia.

Choroidal thinning could therefore be caused by an increase in the sympathetic tone of choroidal vascularization. In normal conditions, choroidal vessels are principally under neurogenic control, and the sympathetic innervation represents a protective mechanism against overperfusion in conditions of acute rise in systemic BP,[8,33] this being able to explain the lack of relationship observed between ChT and BP values in several studies. Hyperactivation of sympathetic nervous system has been widely demonstrated by many authors in arterial hypertension,[34] and previous evidences also showed that increased sympathetic stimuli could impact on renal hemodynamics, with RRI increase induced by sympathetic activation[35] and RRI reduction after renal denervation.[36] In line with this hypothesis, it is similarly conceivable that a chronic increased activation of sympathetic efferences (hypertension-related rather than BP-related) might act on vascular smooth muscle components of choroidal vessels, so influencing the degree of contraction and affect the overall choroidal thickness.

Arterial stiffness, a well-known markers of systemic organ damage and cardiovascular risk in hypertensive subjects,[26] might further represent the link between choroidal vascular damage and impaired renal hemodynamics in this population. Changes in vascular elastic properties can be already apparent in early renal dysfunction,[37] and our group previously demonstrated that aortic pulse wave velocity, the gold standard for arterial stiffness measurement, was significantly and positively associated with intrarenal resistive index in 296 hypertensive subjects with and without impaired renal function[38]; interestingly, this relationship remained statistically significant even after adjustment for BP, eGFR, age, and other covariates, being independent by BP values sensu stricto. As for intrarenal vasculature, it is conceivable that increased arterial stiffness might predispose choroidal circulation to a greater hemodynamic pressure, leading to a choroidal vascular damage and reduced ChT. Moreover, RRI is itself expression of pulsatile flow and reflects systemic extrarenal vascular damage, which could be the effective mediator of morphofunctional choroidal changes.

All these pathophysiological mechanisms could not be mutually exclusive, and other determinants could likely be involved in the complex link between choroidal and renal vasculature such as cigarette smoking, hypercholesterolemia, or other factors[8] involved in early vascular aging; however, further studies are needed to confirm their real role.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Giulio Geraci involved in study conception, study realization, statistics, and manuscript writing. Maria Vadalà, Marta Maria Zammuto and Alessandro Mattina involved in study supervision, statistics, and manuscript supervision. Massimo Castellucci, Giulia Guarrasi, Emilio Nardi, Carlo Maida, Luca Zanoli involved in data collection and analysis, manuscript reviewing, and scientific supervision. Salvatore Cillino and Santina Cottone involved in manuscript reviewing, and scientific supervision. Giuseppe Mulè involved in study conception, manuscript reviewing, and scientific supervision. All authors have approved the final article.

ETHICAL APPROVAL

The study was carried out according to the principles outlined in the Declaration of Helsinki.

Informed consent was signed by all participants.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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