DOI: 10.1111/jch.14195

COMMENTARY

WILEY

Aortic pulsatility drives microvascular organ damage in essential hypertension: New evidence from choroidal thickness assessment

Rosa Maria Bruno MD, PhD[1,2] | Rachel Climie PhD[1,3] | Antonio Gallo MD, PhD[4,5]

[1]INSERM U970, Paris Cardiovascular Research Centre-PARCC, Université de Paris, Paris, France

[2]Pharmacology Unit, Hôpital Européen Georges Pompidou, AP-HP, Paris, France

[3]Baker Heart and Diabetes Institute, Melbourne, Australia

[4]Department of Endocrinology and Prevention of Cardiovascular Disease, Institute of Cardio Metabolism And Nutrition (ICAN), La Pitié-Salpêtrière Hospital, AP-HP, Paris, France

[5]Laboratoire d'imagerie Biomédicale, INSERM, CNRS, Sorbonne University, Paris, France

Correspondence: Rosa Maria Bruno, INSERM U970 Team 7, Paris Cardiovascular Research Centre–PARCC, Université de ParisAP-HP, Pharmacology Unit, Hôpital Européen Georges Pompidou, 56 Rue Leblanc, 75015 Paris, France.
Email: rosa-maria.bruno@inserm.fr

Funding information
REC is supported by an Australian National Heart Foundation Postdoctoral Fellowship.

1 | INTRODUCTION

In a healthy cardiovascular system, the compliant properties of the large arteries ensure that pulsations in pressure and flow generated by cyclic left ventricular contraction are dampened at the site of the ascending aorta into a continuous pressure (and flow) downstream at the site of arterioles. This allows for the delivery of a steady flow of blood during organ perfusion, and the microvasculature of target organs is protected from the damaging effects of pressure pulsatility.[1] The dampening of the pressure/flow is achieved via the windkessel effect whereby the aorta expands during systole and temporarily stores a portion of the stroke volume, which is then propelled into the systemic circulation during diastole via recoil of the elastic arterial wall. However, in response to aging, hypertension, and other disease states, arterial stiffening limits the buffering capacity of the elastic arteries. The wear-and-tear of elastic fibers in the aortic wall, due to the mechanical stress induced by each heartbeat, is amplified by high blood pressure.[2] This results in increased transmission of pulsatile pressure/flow to the microvasculature of target organs, which may lead to capillary rarefaction, ischemia, and ultimately, target organ damage.[3-6]

Microvascular damage in hypertension has been demonstrated by invasive techniques in humans, mostly as increased media-lumen ratio, the so-called eutrophic remodeling.[7,8] However, it is now possible to image directly and non-invasively the microcirculation in the retina.[9] Non-invasive near-histological analysis of retinal microcirculation confirmed in vivo the impact of systolic and pulse pressure on arteriolar wall thickness and wall cross-sectional area, suggesting arteriolar hypertrophy as a consequence of an increased pulsatile stress.[10]

More recently, novel accurate and non-invasive techniques have allowed evaluating the anatomy and function of another important vascular layer: the choroid. The inner retinal and choroidal vasculature are completely independent vascular systems, and present specific anatomical and physiological peculiarities. The anatomical configuration of the choroid is very intricate, including up to 5 separate layers, containing different types of vessels: From the terminal branches of posterior ciliary arteries, some "feeder" arterioles are connected to the choriocapillaris in a triangular pattern, making of choroidal vasculature an end-arterial circulation.[11] As a result of this complex organization, the choroid received 80% of blood supply from systemic circulation, compared to 5% of the retina; furthermore, the choroidal vasculature is less protected and autoregulated

than the retinal one.[12] Thus, it is conceivable that choroidal vasculature is largely affected by the pulsatility transmitted by large vessels.

This hypothesis is confirmed by Mulé and coauthors in the present issue of Journal of Clinical Hypertension.[13] In this paper, Mulé explored choroidal thickness in 155 hypertensive patients undergoing a 24-hour ambulatory blood pressure monitoring for the evaluation of central and brachial 24 hour-pulse pressure.[14] Patients with a central pulse pressure > 35 mm Hg exhibited a thinner choroidal thickness. These individuals were older, had a worse renal function, and showed higher systolic central and peripheral blood pressure. However, pulse pressure (central > peripheral) was the only predictor of choroidal thickness impairment, independent of confounders.

In this study, choroidal thickness was evaluated by optic computed tomography-angiography, one of the most innovative techniques for the evaluation of microvascular flow in deeper retinal structures.[9,15] However, some technical limitations of the technique need to be acknowledged. It is still difficult to distinguish the many vascular contributors of this complex vascular layer, even with ameliorated techniques as the swept-source used in the study. Furthermore, signal attenuation may be difficult to overcome when it comes to the detailed structural analysis. This lack of specificity makes it difficult to clearly define physiopathological mechanisms underlying changes in choroidal thickness in hypertension, which may be induced either by capillary rarefaction (as demonstrated in the retina[16]) or by small muscular artery vasoconstriction from the deeper vascular layers, as well as by non-vascular smooth muscle contraction. Neighbor structures as the retinal pigment epithelium, involved in the crosstalk with choriocapillaris, may also play a role.[17]

In conclusion, the provided results indicate a strong association between 24-hour central pulse pressure and choroidal thickness in essential hypertensive patients. Large population studies have shown that choroidal structural remodeling is largely influenced by aging.[18] These results shed a new light on this phenomenon, indicating that age-induced changes in central hemodynamics are most likely responsible for choroidal thickness reduction. Further research is needed to elucidate the mechanisms responsible and the anatomical structures involved in the hypertensive choroidal phenotype.

ACKNOWLEDGEMENT

None.

DISCLOSURES

AG has received honoraria for public speaking or consultancy support from Akcea Therapeutics, AMGEN, Mylan, Novartis, Sanofi and Regeneron, Unilever, and MSD. The other authors have nothing to disclose.

ORCID

Rosa Maria Bruno https://orcid.org/0000-0002-6107-3356

REFERENCES

1. Boutouyrie P, Bruno RM. The clinical significance and application of vascular stiffness measurements. *Am J Hypertens*. 2019;32:4-11.
2. O'Rourke MF, Hashimoto J. Mechanical factors in arterial aging: a clinical perspective. *J Am Coll Cardiol*. 2007;50:1-13.
3. Rosenbaum D, Mattina A, Koch E, et al. Effects of age, blood pressure and antihypertensive treatments on retinal arterioles remodeling assessed by adaptive optics. *J Hypertens*. 2016;34:1115-1122.
4. Climie RE, van Sloten TT, Bruno RM, et al. Macrovasculature and microvasculature at the crossroads between type 2 diabetes mellitus and hypertension. *Hypertension*. 2019;73:1138-1149.
5. Bruno RM, Cartoni G, Stea F, et al. Carotid and aortic stiffness in essential hypertension and their relation with target organ damage: the CATOD study. *J Hypertens*. 2017;35:310-318.
6. Rezaeian M, Mojtaba Golzan S, Avolio AP, Graham S, Butlin M. The association between retinal and central pulse wave velocity in the elderly. *Artery Res*. 2020;26:148-153.
7. Bruno RM, Grassi G, Seravalle G, et al. Age- and sex-specific reference values for media/lumen ratio in small arteries and relationship with risk factors. *Hypertension*. 2018;71:1193-1200.
8. Bruno RM, Duranti E, Ippolito C, et al. Different impact of essential hypertension on structural and functional age-related vascular changes. *Hypertension*. 2017;69:71-78.
9. Climie RE, Gallo A, Picone DS, et al. Measuring the interaction between the macro- and micro-vasculature. *Front Card Med*. 2019;6:169.
10. Gallo A, Dietenbeck T, Giron A, Paques M, Kachenoura N, Girerd X. Non-invasive evaluation of retinal vascular remodeling and hypertrophy in humans: intricate effect of ageing, blood pressure and glycaemia. *Clin Res Cardiol*. 2020. [Epub ahead of print].
11. Lee JE, Ahn KS, Park KH, et al. Functional end-arterial circulation of the choroid assessed by using fat embolism and electric circuit simulation. *Sci Rep*. 2017;7:2490.
12. Chaine G, Imbs JL.*Rappel Anatomo-Physiologique Des Particularités De La Circulation Oculaire*.In: Flament J, Storck D ed. Masson: OEil et pathologie générale Paris, 1997:127-138.
13. Mulè G, Vadalà M, Sinatra N, et al. Relationship of choroidal thickness with pulsatile hemodynamics in essential hypertensive patients. *J Clin Hypertens (Greenwich)*. 2021;23(5):1030–1038.
14. Kotovskaya YV, Kobalava ZD, Orlov AV. Validation of the integration of technology that measures additional "vascular" indices into an ambulatory blood pressure monitoring system. *Med Devices (Auckl)*. 2014;7:91-97.
15. Borrelli E, Sarraf D, Freund KB, Sadda SR. OCT angiography and evaluation of the choroid and choroidal vascular disorders. *Prog Retin Eye Res*. 2018;67:30-55.
16. Bosch AJ, Harazny JM, Kistner I, Friedrich S, Wojtkiewicz J, Schmieder RE. Retinal capillary rarefaction in patients with untreated mild-moderate hypertension. *BMC Cardiovasc Disord*. 2017;17:300.
17. Blaauwgeers HG, Holtkamp GM, Rutten H, et al. van Hinsbergh VW and Schlingemann RO. Polarized vascular endothelial growth factor secretion by human retinal pigment epithelium and localization of vascular endothelial growth factor receptors on the inner choriocapillaris. Evidence for a trophic paracrine relation. *Am J Pathol*. 1999;155:421-428.
18. Schuster AK, Leuschner A, Feretos C, et al. Choroidal thickness is associated with cardiovascular risk factors and cardiac health: the Gutenberg Health Study. *Clin Res Cardiol*. 2020;109:172-182.

How to cite this article: Bruno RM, Climie R, Gallo A. Aortic pulsatility drives microvascular organ damage in essential hypertension: New evidence from choroidal thickness assessment. *J Clin Hypertens*. 2021;23:1039–1040. https://doi.org/10.1111/jch.14195