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Short Communication

Evoking Awareness toward Muscular Arterial Remodeling and Stiffness

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1. INTRODUCTION

The leading cause of this report is that for many years the focus of clinical research was directed mainly toward large arteries remodeling. In the past decade the assessment of microcirculatory function was introduced [1] outlining its importance in cardiovascular risk stratification. However, the remodeling of arteries in-between, muscular arteries, is still poorly understood. Actually, there is no doubt that central arterial stiffness is an independent predictor of cardiovascular events, cardiovascular and all-cause mortality [2,3], and even target organ damage [4,5]. Besides, non-invasively measured central arterial stiffness [carotid-femoral pulse wave velocity (cfPWV)] strongly correlates with invasively measured aortic arterial stiffness [6]. Though, by using this approach there is a risk to develop rather fragmental attitude to arterial tree and to miss the remodeling patterns in the whole branching system of arteries. The aim of this report is to evoke awareness and interest towards peripheral muscular arteries remodeling.

The complexity of elastic and muscular arteries wall has been well-described previously [7]. Aging results in elastin degradation and pronounced collagen synthesis with deposition in arterial wall. This process is accompanied by the activation, proliferation and migration of Vascular Smooth Muscle Cells (VSMCs), endothelium dysfunction and altered extracellular matrix [8]. Elastic arteries produce more basal nitric oxide [9] and are able to stretch and compensate pressure waves from the left ventricle. On the other hand, muscular arteries seem to be less affected by age [10]. Reasons for that are not properly understood. Tunica media layer of peripheral muscular arterial wall is very rich in VSMCs, whereas, tunica intima is poor in elastic fibers [9], thus, elastin degradation process here is not so pronounced. In comparison to elastic arteries, VSMCs are more elongated and narrower, therefore, have better ability to contract and serve for pulse-smoothening [11].

Aging related geometrical remodeling along arterial tree is inconsistent. The expert reports [12] usually suggest to measure central arterial stiffness as the superior marker for CV risk assessment [13]. Some of the researchers oppose this opinion and use other indexes, for example, the calculation of mismatch between elastic and muscular arteries (carotid-femoral PWV divided by carotid-radial PWV). The downside is that this ratio has limited performance in general population and is more specific to certain cohorts: chronic kidney disease (CKD) [14,15], diabetes [16], female gender [17] (with high cardiovascular risk profile) and related to male sexual function [18]. Analysis of cardiologic ambulatory patients [10] revealed unchanged aging related arterial stiffness in muscular arteries, but increased pulse wave velocity mismatch, suggesting the link to end-organ damage. The results of all studies are inconsistent, but it implies that increased mismatch could be related to altered microvasculature function.

By sticking to the idea that peripheral arterial stiffness is a poor predictor of CV risk and all-cause mortality [19] we are missing the whole picture. Interesting data were published by Bortolotto et al. [13]. They have measured Intima Media Thickness (IMT) in both the carotid and radial arteries. Aging resulted in more pronounced IMT thickening in carotids. However, further works [20] revealed that high-resolution radial IMT can compete against carotid IMT in evaluating arterial remodeling burden and that it is also related to previous cardiovascular disease (CVD) and ischemia. An interesting study in renal artery biopsies reported a positive relationship between renal arteriosclerosis and augmentation index, a surrogate for peripheral arterial stiffness [21]. The main limitation of this study was borderline subject age for better performance of augmentation index [12].

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It is worthwhile noting that one of the main players in arterial remodeling is the response to wall shear stress, which induces swelling and proliferating of endothelial cells [22]. Further, endothelial cells release chemotactic compounds and inflict inflammatory response leading to activation of VSMCs. The behavior of VSCMs and their transdifferentiation will be discussed later in this report. Shear stress is not always a "bad player" [22], especially in the context of exercise-induced arterial adaptation, as it enhances peripheral function. A study [23] with 10 young healthy men applied low flow-mediated (L-FMC) vasodilatation technique during acute dynamic exercise with a large muscle mass and registered post-exercise augmentation of the radial artery L-FMC response. Authors suggest that this enhanced vasoconstriction might explain increased post-exercise cardiovascular risk, because it might mimic coronary artery response. Moreover, due to nonuniform wall shear stress thorough whole arterial tree [24] is atherosclerosis [25] more pronounced in lower extremities conduit arteries. This shows clearly that muscular arterial remodeling is highly dependent on the site.

Muscular arteries remodel mainly longitudinally, this induce increase in intima-to-media thickness and endothelial dysfunction [26]. On account of the fact that there are no interventional studies which measured muscular arterial stiffness directly and compared it to non-invasive methods, caution should be taken when analyzing peripheral pulse wave velocity. There is no assurance that measurement of carotid-femoral PWV or femoral-distal PWV fully correspond the actual arterial stiffness. Calculation of pulse wave velocity depends on the distance and pulse transit time [27]. Besides, the length (distance) of the arteries is age predetermined. In other words, both in muscular and elastic arteries aging results in increased length and tortuosity [28], however, muscular arteries does not increase in diameter. Therefore, the accuracy of measuring technique of distance between two muscular arteries pulse sites could be mistaken. Invasive studies of peripheral arterial stiffness and/or methods for better measurement of pulse transit distance are suggested.

It is important to mention one of crucial arterial remodeling aspects - vascular calcification (VC). VC appears mainly as medial calcification in muscular arteries [29]. Medial calcification is the result of VSMCs apoptosis and transdifferentiation to osteoblasts and therefore ectopic VC [10]. These changes lead to diminished ability to properly contract and to altered arterial resistance. This hypothesis might be supported by lower peripheral pulse pressure values in elderly people [30] and by increased mismatch between elastic and peripheral arterial stiffness observed in CKD [16] and etc. Nevertheless, medial calcification has been attributed to normal aging, diabetes mellitus, CKD and obstructive sleep apnea [29].

The crosstalk of peripheral arterial remodeling and early life factors should be elucidated. A study on 2856 subjects showed that AIx is inversely associated with birth weight and participants born Small for Gestational (SGA) age had even higher values of augmentation index (Aix) [31]. However, other previous researchers could not confirm this link [32] and noticed no difference in carotid media intima thickness in regard of SGA [33]. There is still a need to further explanation how early life factors affect the whole arterial branching system.

In conclusion, the meaning of peripheral arterial remodeling and stiffness is poorly understood. We should not forget that aging is not a local process, but affects the whole arterial tree. Muscular arteries become longer, more turtous and increase in wall to lumen ratio. By learning lessons from peripheral arteries we could find the missing puzzle pieces of normal and accelerated arterial aging. Future studies should target relationship of peripheral arterial remodeling and early life factors. More accurate solutions in measuring arterial stiffness in periphery and invasive validation of these methods are also encouraged.

REFERENCES

[1] Tibiriçá E, De Lorenzo A, de Oliveira GMM. Microcirculation and cardiovascular diseases. Arq Bras Cardiol 2018;111:120–1.

[2] Mattace-Raso FUS, van der Cammen TJM, Hofman A, van Popele NM, Bos ML, Schalekamp MADH, et al. Arterial stiffness and risk of coronary heart disease and stroke. Circulation 2006;113:657–63.

[3] Ben-Shlomo Y, Spears M, Boustred C, May M, Anderson SG, Benjamin EJ, et al. Aortic pulse wave velocity improves cardiovascular event prediction: an individual participant meta-analysis of prospective observational data from 17,635 subjects. J Am Coll Cardiol 2014;63:636–46.

[4] Vasan RS, Short MI, Niiranen TJ, Xanthakis V, DeCarli C, Cheng S, et al. Interrelations between arterial stiffness, target organ damage, and cardiovascular disease outcomes. J Am Heart Assoc 2019;8:e012141.

[5] Scuteri A, Morrell CH, Fegatelli DA, Fiorillo E, Delitala A, Orru' M, et al. Arterial stiffness and multiple organ damage: a longitudinal study in population. Aging Clin Exp Res 2019;1–8.

[6] Whitlock MC, Hundley WG. Noninvasive imaging of flow and vascular function in disease of the aorta. JACC Cardiovasc Imaging 2015;8:1094–106.

[7] Tucker WD, Mahajan K. Anatomy, blood vessels. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 (Updated January 4, 2019).

[8] Cunha PG, Boutouyrie P, Nilsson PM, Laurent S. Early vascular ageing (EVA): definitions and clinical applicability. Curr Hypertens Rev 2017;13:8–15.

[9] Leloup AJA, Van Hove CE, Heykers A, Schrijvers DM, De Meyer GRY, Fransen P. Elastic and muscular arteries differ in structure, Basal NO production and voltage-gated Ca^{2+}-channels. Front Physiol 2015;6:375.

[10] Zhang Y, Agnoletti D, Protogerou AD, Topouchian J, Wang JG, Xu Y, et al. Characteristics of pulse wave velocity in elastic and muscular arteries: a mismatch beyond age. J Hypertens 2013;31:554–9.

[11] Safar ME. Can antihypertensive treatment reverse large-artery stiffening? Curr Hypertens Rep 2010;12:47–51.

[12] Townsend RR. Arterial stiffness: recommendations and standardization. Pulse (Basel) 2017;4:3–7.

[13] Bortolotto LA, Hanon O, Franconi G, Boutouyrie P, Legrain S, Girerd X. The aging process modifies the distensibility of elastic but not muscular arteries. Hypertension 1999;34:889–92.

[14] Safar ME, Plante GE, Mimran A. Arterial stiffness, pulse pressure, and the kidney. Am J Hypertens 2015;28:561–9.

[15] Safar ME, Thomas F, Blacher J, Nzietchueng R, Bureau JM, Pannier B, et al. Metabolic syndrome and age-related progression of aortic stiffness. J Am Coll Cardiol 2006;47:72–5.

[16] Fortier C, Agharazii M. Arterial stiffness gradient. Pulse (Basel) 2016;3:159–66.

[17] Laucyte-Cibulskiene A, Vickiene A, Ryliskyte L, Badariene J, Rimsevicius L, Miglinas M. Should we calculate arterial stiffness

gradient in middle-aged women with increased cardiovascular risk? Blood Press 2019;28:199–205.
[18] Kumagai H, Yoshikawa T, Myoenzono K, Kosaki K, Akazawa N, Asako ZM, et al. Sexual function is an indicator of central arterial stiffness and arterial stiffness gradient in Japanese adult men. J Am Heart Assoc 2018;7:pii: e007964.
[19] Ye C, Pan Y, Xu X, Su S, Snieder H, Treiber F, et al. Pulse wave velocity in elastic and muscular arteries: tracking stability and association with anthropometric and hemodynamic measurements. Hypertens Res 2016;39:786–91.
[20] Eklund C, Friberg P, Gan LM. High-resolution radial artery intima-media thickness and cardiovascular risk factors in patients with suspected coronary artery disease – comparison with common carotid artery intima-media thickness. Atherosclerosis 2012;221:118–23.
[21] Li Y, Yang Y, Wang W, Miao H, Zhang L, Cai G, et al. Peripheral arterial stiffness is correlated with intrarenal arteriolosclerosis according to biopsies from patients with kidney disease. Nephrology (Carlton) 2019.
[22] Silver AE, Vita JA. Shear stress–mediated arterial remodeling in atherosclerosis: too much of a good thing? Circulation 2006;113:2787–9.
[23] Elliott RO, Alsalahi S, Fisher JP. Impact of acute dynamic exercise on radial artery low-flow mediated constriction in humans. Eur J Appl Physiol 2018;118:1463–72.
[24] Wu SP, Ringgaard S, Oyre S, Hansen MS, Rasmus S, Pedersen EM. Wall shear rates differ between the normal carotid, femoral, and brachial arteries: an in vivo MRI study. J Magn Reson Imaging 2004;19:188–93.
[25] Laclaustra M, Casasnovas JA, Fernández-Ortiz A, Fuster V, León-Latre M, Jiménez-Borreguero LJ, et al. Femoral and carotid subclinical atherosclerosis association with risk factors and coronary calcium: the AWHS study. J Am Coll Cardiol 2016;67:1263–74.
[26] Thijssen DHJ, Carter SE, Green DJ. Arterial structure and function in vascular ageing: are you as old as your arteries? J Physiol 2016;594:2275–84.
[27] Measurement of aortic stiffness | European Society of Hypertension. Available from: https://www.eshonline.org/annual-meeting-posts/measurement-of-aortic-stiffness/ (Accessed November 28, 2019)
[28] Man AWC, Wang Y. Age-associated arterial remodelling. EC Cardiol 2017;4:137–64.
[29] Tsai CW, Kuo CC, Hwang JJ. Mönckeberg's sclerosis. Acta Clin Belg 2010;65:361.
[30] McEniery CM, Yasmin, Hall IR, Qasem A, Wilkinson IB, Cockcroft JR. Normal vascular aging: differential effects on wave reflection and aortic pulse wave velocity: the Anglo-Cardiff Collaborative Trial (ACCT). J Am Coll Cardiol 2005;46:1753–60.
[31] Sperling J, Nilsson PM. Does early life programming influence arterial stiffness and central hemodynamics in adulthood? J Hypertens 2019;37:e94.
[32] Miles KL, McDonnell BJ, Maki-Petaja KM, Yasmin, Cockcroft JR, Wilkinson IB, et al. The impact of birth weight on blood pressure and arterial stiffness in later life: the Enigma study. J Hypertens 2011;29:2324–31.
[33] Stock K, Schmid A, Griesmaier E, Gande N, Hochmayr C, Knoflach M, et al. The impact of being born preterm or small for gestational age on early vascular aging in adolescents. J Pediatr 2018;201:49.e1–54.e1.