Review article

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Measuring methods of blood pressure and arterial stiffness
A new approach

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ABSTRACT

Carotid-femoral pulse wave velocity (c-f PWV) is considered to be one of the main factors affecting CV risk in the hypertensive population and has been included to the detailed screening of the hypertensive patients according to the ESH guidelines. Despite the large number of studies proving the correlation of blood pressure (BP) and c-f PWV as well as arterial stiffness, there are only few studies to show which BP measurement method can better predict arterial stiffness. Generally, these studies express the superiority of ABPM in the prediction of c-f PWV and early vascular aging (EVA). Furthermore, while guidelines recommend measuring c-f PWV in the hypertensive population, on the other hand it is difficult, time consuming and expensive to measure arterial stiffness in the everyday clinical practice, limiting its use only for experts. These limitations lead to the creation of a new score, the Early Vascular Aging Ambulatory score (EVAAs), which uses parameters from the ABPM and other cardiovascular risk factors in order to identify the possibility of each patient to have EVA. The score should be further studied for its accuracy in a larger population, as well for predicting hard end points in prospective studies.

KEY WORDS: *Hypertension, home blood pressure, office blood pressure, ambulatory blood pressure monitor, arterial stiffness, early vascular aging ambulatory score*

INTRODUCTION

The importance of hypertension-mediated organ damages (HMOD) gained a significant place in the latest 2018 ESH guidelines, replacing recently the term 'target organ damage'.[1] This new term aims to a more essential description of the structural and functional changes in different hypertension-affected organs such as heart, kidneys and vessels. HMOD should be taken into account not only for the management but also for the evaluation of cardiovascular (CV) risk of the hypertensive patient. The reason is simply the fact that HMOD are not included in the different scores for the evaluation of CV risk, concluding to the underestimation of the risk in a large part of hypertensive patients.

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Arterial stiffness, measured either by pulse pressure (in older people) or by carotid-femoral pulse wave velocity (c-f PWV), is considered to be one of the main factors affecting CV risk in the hypertensive population and has been included to the detailed screening of the hypertensive patients. Indeed, it has been placed in the same concernment with other important asymptomatic HMOD such as left ventricular hypertrophy, microalbuminuria, moderate chronic kidney disease, advanced retinopathy and ankle-brachial index.[1] Maybe, this was expected if we consider that c-f PWV has been recognized all these years as the gold standard of measuring arterial stiffness.[2] Furthermore, a large number of trials and meta-analyses have been focused on indentifying and finally proving the relationship of arterial stiffness and CV events.[3-6] This fact stabilizes the importance of arterial stiffness, especially in the hypertensive population.

While arterial stiffness has been established, especially in the field of research, two main topics remain unidentifiable. First of all, which measuring method of blood pressure (BP) can better predict c-f PWV damage should be clarified. Moreover, guidelines recommend measuring c-f PWV in the hypertensive population, but on the other hand refer that the measurement of arterial stiffness is difficult in the everyday clinical practice, limiting its use only for experts.

IMPORTANCE OF ARTERIAL STIFFNESS MEASURED AS C-F PWV

Carotid arterial stiffness has been associated with several CV risk factors such as increasing age,[7] hypertension,[8,9] diabetes mellitus[10,11] and dyslipidemia.[12] Other parameters related to CV disease have been also found to be connected with increased arterial stiffness. These factors are metabolic syndrome,[13] non-alcoholic fatty liver disease,[14] hyperuricemia[15] and chronic kidney disease.[16]

Except from the association of carotid-femoral arterial stiffness with CV risk factors, data shows its association also with CV events and mortality. Carotid arterial stiffness studied firstly by Blacher J et al,[17] who provided evidence about its correlation as an independent determinant with all-cause and CV mortality in patients with end-stage renal disease. The same results were confirmed even in renal transplant recipients,[6] while recently a study with a larger number of patients with chronic kidney disease and a significant follow-up period showed that c-f PWV is a significant predictor of the progression of kidney disease and death in this population.[18] Translating these results, c-f PWV measurements seems to help define better the risks for these important health outcomes in patients with chronic kidney disease. The Hoorn Study evaluated different measuring methods of arterial stiffness for their correlation with mortality and morbidity. In the general population, it seems that c-f PWV can better predict CV events and all-cause mortality compared with other stiffness parameters such as brachial stiffness, augmentation index, and systemic arterial compliance, even after adjustment for CV risk factors.[19] The latest systematic review and meta-analysis studding the c-f PWV in the prediction of CV events showed that higher the c-f PWV values equals with higher risk of CV events and mortality. Moreover, it seems that the predictive value of increased arterial stiffness was higher in patients with higher disease risk for total CV events and CV mortality than in other patients.[3] The above studies confirm the importance of carotid-femoral arterial stiffness as a biomarker for the prediction of CV risk and identification of high-risk populations, such as the hypertensives.

WHICH MEASURING METHOD OF BP CAN BETTER PREDICT ARTERIAL STIFFNESS?

Studies usually evaluate the correlation between BP and arterial stiffness with the use of office BP, while studies with home and ABPM measurements are rare. Despite the considerable number of studies dealing with arterial stiffness as BP target organ damage, there are only few studies comparing which BP measuring method (office, home, ambulatory BP monitor (ABPM)) better predict the arterial stiffness, especially when this is measured as c-f PWV.

At 2003, Calvo-Vargas C et al showed that loaned self-measurements of BP are correlated better with c-f PWV, compared with the readings taken in the office.[20] In the Finn-Home Study, home BP found to be one of the most important factors affecting arterial stiffness. Home-measured BP was more strongly associated with c-f PWV than clinic BP, even for a low number of measurements.[21] To our knowledge, there are only two studies evaluating ABPM and office BP for their correlation with arterial stiffness. Stergiou et al[22] compared the three different BP measurement methods in predicting hypertensive target organ damage (left-ventricular mass index, urinary albumin excretion rate, and c-f PWV). The results of this study showed no statistically significant correlation between c-f PWV and different BP measurements, a finding that is in contrast with studies suggesting a relationship of arterial stiffness with SBP.[4,8] On the other hand, the second existing study showed a statistically significant correlation with c-f PWV and all the parameters of ABPM (systolic BP, diastolic BP, heart rate) in the multivariate analysis, where office and home BP did not remain statistically significant determinants of arterial stiffness.[23] This study is the only one which also compares

the three measuring methods of BP with early vascular aging (EVA). EVA, defined from arterial stiffness, represents an accelerated state of vascular aging, not compatible with patient's chronological age.[24,25] Similarly, systolic BP from ABPM found to predict better EVA compared with systolic BP from home or office.[23] No other studies were found for the predictive value of different BP measuring methods (office, home, ABPM) on the identification of carotid-femoral arterial stiffness and EVA in hypertensive patients. The results of the literature indicate the need for further investigation in this field, but generally express the superiority of ABPM in the prediction of c-f PWV and EVA.

DIFFICULTY IN THE ESTIMATION OF C-F PWV AND EVA

According to the Artery Society and the ESH Working Group on Vascular Structure and Function recommendations,[26] the examination of measuring c-f PWV should be taken place in a quiet laboratory with constant temperature at 21° C. The patient remains in a supine position for at least 10 minutes before the examination, while caffeine, smoking and food are not allowed within 3 hours before the measurement. Additionally, it is recommended the same physician to repeat the measurement ten minutes after the first measurement. If difference between the two measurements is more than 0.5 m/s, a third measurement should be performed. The average of these measurements is used to calculate c-f PWV. C-f PWV is calculated by dividing the 80% of direct distance between the recording sites (carotid-femoral) with the transit time of the arterial pulse along the distance.[2] The transit time is obtained by the system automatically, while the distances are measured by the researcher using a centimeter tape.[27] Finally, EVA is defined as c-f PWV values higher than the expected for age average values according to European population data.[28] All the above make the measurement difficult, time consuming and realizable only from experts for research purpose. Moreover, it is extremely expensive if we consider the cost for the equipment as well as the consumables.

In the past, there was a try to calculate arterial stiffness from parameters of ABPM, the known ambulatory arterial stiffness index (AASI). AASI was designed as a predictor of arterial stiffness, taking into account that elasticity in the arterial system influences the height of the diastolic BP as well as its relation to systolic BP.[29] ASSI found to be an easy way to estimate arterial stiffness not only in the field of research but also in daily practice. The main disadvantage of this score is that important predictors of vascular age have not been considered. AASI is strongly dependent on the degree of nocturnal BP fall in hypertensive patients and there is no significant relation between AASI and left ventricular mass after proper adjustment for confounders. Moreover, the relation between AASI and a widely accepted measure of aortic stiffness, such as pulse wave velocity, is weak and importantly affected by other factors.[30] Despite these limitations, studies have shown significant relationship between AASI and CV events and mortality.[31-33]

In order to overcome the difficulty in the calculation of c-f PWV and EVA, to minimize the cost and to find an easy way to evaluate HMOD in the hypertensive population in daily practice, we recently create a new score the Early Vascular Aging Ambulatory score (EVAAs).[23] After proving that ABPM can better be correlated with c-f PWV compared to home and clinic BP measurements and better predict EVA, we moved a step forward. Random Forest algorithm was used to identify multiple parameters for the prediction of EVA. According to the Gini importance, 24h systolic and diastolic BP, 24h heart rates, age, sex, body mass index, diabetes mellitus (yes/no), and estimated glomerular filtration rate (eGFR) were used to develop a new score for EVA providing a total accuracy of 0.82, 0.84 sensitivity and 0.78 specificity. Other parameters such as treatment, waist, hip, smoking and lipids levels were excluded from the score because they were not statistically significant. The EVAAs of each patient can practically be calculated with the use of an application.[23] The advantage of this score is the great accuracy, sensitivity and specificity that offers and the simultaneous use of different parameters, that have been proved to affect arterial stiffness, in order to finally evaluate the possibility of each patient to have EVA. Furthermore, the choice of Random Forest algorithm, a supervised machine learning, provides the advantage of cross-validation in an independent population and as a result the generalization of the result.[34] The only disadvantage of this score is the need of internet connection for the access to the application, which is totally free.

CONCLUSION

C-f PWV has been established as an important factor affecting CV risk in the hypertensive population and has been included to the detailed screening of the hypertensive patients, according to the ESH guidelines. Indeed, its use is recommended not only for research, but also more significantly in daily practice. ABPM seems to predict better the arterial stiffness compared to clinic and home BP measurements. The new score, EVAAs, combines different parameters from the ABPM with CV risk factors and identifies the possibility of a patient to have EVA. EVAAs model should be further evaluated for its accuracy in a larger population, as well for predicting CV events and mortality in prospective studies. Moreover, EVAAs should

be evaluated for its performance on other hypertensive target organs. Finally, in the future the prediction of EVA, assessed by EVAAs, could be used in the management of hypertensive patients in order to prevent future CV events.

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ΠΕΡΙΛΗΨΗ

Μέθοδοι μέτρησης της αρτηριακής πίεσης και της αρτηριακής σκληρίας Μία νέα προσέγγιση

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Η καρωτιδο-μηριαία ταχύτητα σφυγμικού κύματος θεωρείται ένας από τους βασικούς παράγοντες καρδιαγγειακού κινδύνου στον υπερτασικό πληθυσμό και συμπεριλαμβάνεται στον λεπτομερή έλεγχο των υπερτασικών ασθενών βάση των κατευθυντήριων οδηγιών της Ευρωπαϊκής Εταιρίας Υπέρτασης. Παρόλο το μεγάλο αριθμό μελετών που αποδεικνύουν τη συσχέτιση της αρτηριακής πίεσης (ΑΠ) και της καρωτιδο-μηριαίας ταχύτητας σφυγμικούς κύματος, ελάχιστες είναι οι μελέτες που ελέγχουν ποια μέθοδος μέτρησης της ΑΠ μπορεί να προβλέψει καλύτερα την αρτηριακή σκληρία. Σε αυτές τις μελέτες φαίνεται πως η 24η καταγραφή της ΑΠ υπερέχει. Επιπλέον, ενώ οι κατευθυντήριες οδηγίες συστήνουν τη μέτρηση της καρωτιδο-μηριαίας ταχύτητας σφυγμικού κύματος στον υπερτασικό πληθυσμό, η μέτρηση είναι δύσκολη, χρονοβόρα και ακριβή στην καθ' ημέρα κλινική πράξη, περιορίζοντας τη χρήση της κυρίως για ερευνητικό σκοπό. Αυτοί οι περιορισμοί οδήγησαν στη δημιουργία ενός νέου μοντέλου, το Early Vascular Aging Ambulatory score (EVAAs), που χρησιμοποιεί παραμέτρους από την 24ωρη καταγραφή της ΑΠ και άλλους παράγοντες καρδιαγγειακού κινδύνου για να ανιχνεύσει ασθενείς με πρώιμη αγγειακή γήρανση. Το μοντέλο αυτό πρέπει να μελετηθεί περαιτέρω σε μεγαλύτερο πληθυσμό, καθώς και για την πιθανή συσχέτιση του με τελικά καταληκτικά σημεία.

ΛΕΞΕΙΣ ΚΛΕΙΔΙΑ: *Υπέρταση, αρτηριακή πίεση στο σπίτι, αρτηριακή πίεση ιατρείου, 24ωρη περιπατητική καταγραφή της αρτηριακής πίεσης, αρτηριακή σκληρία*

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