Introduction to the Eighth International Workshop on Structure and Function of the Vascular System

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The Eighth International Workshop on Structure and Function of the Vascular System was held in Paris, France, from February 16 through February 18, 2012. In the first editions of this workshop during the 1990s, the focus was on methodologies to assess vascular structure and function in humans, as well as how these changes contribute to cardiovascular risk. We now have well-standardized approaches to assess both large artery and microvascular structure and function. Thus, the focus of the workshop has shifted toward mechanistic studies on how mechanical factors affect arterial remodeling and target-organ damage. In addition, the question of whether pulse wave velocity is an adequate marker for (cardio)vascular disease can now be raised with more experimental evidence to find an answer.

During the 3-day symposium, 5 sessions were held. The first dealt with arterial mechanical properties and target-organ damage. In recent years, most therapeutic trials have been focused on their own specific topic, diabetes mellitus or hypertension or hypercholesterolemia. Studies associating several cardiovascular risk factors have been performed only to a limited degree. The most frequent association refers to hypertension and diabetes mellitus type 2. Each of these 2 cardiovascular risk factors increases independently arterial stiffness, but the association has never been specifically investigated in humans. Factors associated with arterial stiffness differ markedly in hypertension (age, blood pressure [BP], and heart rate) and diabetes mellitus (advanced glycation end products and insulin resistance). Michel Safar showed that, for the same mean arterial BP, arterial stiffness is much higher in diabetes mellitus than in hypertension. On the other hand, the risk of stroke is much higher in hypertension and diabetes mellitus than in hypertension. The risk of stroke is much higher in diabetes mellitus than in hypertension. On the other hand, the risk of stroke is much higher in hypertension and diabetes mellitus than in hypertension. The risk of stroke is much higher in diabetes mellitus than in hypertension. The risk of stroke is much higher in diabetes mellitus than in hypertension. On the other hand, the risk of stroke is much higher in hypertension and diabetes mellitus than in hypertension.

Nico Westerhof and Michael O’Rourke provided evidence in this workshop that the association of hypertension and diabetes mellitus requires the reduction of arterial stiffness but also of wave reflections. Westerhof proposed a model associating compliance, resistance, and inerterance and O’Rourke a model related to pulse pressure amplification.

Athanase Protagou discussed how the noninvasive assessment of 24-hour aortic ambulatory BP provided the opportunity to investigate the interaction between the time-dependence and arterial site-dependence of BP variability. In addition, in the study of Weber et al., a novel method for the assessment of wave reflections based on an adopted Windkessel model, a flow curve estimation from the radial pressure waveforms, and wave separation analysis was applied in patients undergoing coronary angiography. The amplitude of reflected wave was significantly associated with the combined effects of cardiovascular end points. Clearly, such methods improve substantially the accuracy of cardiovascular assessments. In the last presentation of this session, Véronique Regnault suggested that hypertension and diabetes mellitus may confer, per se, a hypercoagulable state only because the main observed complications are stroke and myocardial infarction. She showed that, in spontaneous hypertension, there is an increase of vascular synthesis of tissue factor and tissue factor pathway inhibitor. Furthermore, vascular smooth muscle cells of spontaneously hypertensive rats confer a prothrombotic phenotype.

The next 2 sessions dealt with arterial remodeling, inflammation, and microcirculation, with a particular focus on eclampsia. Ernesto Schiffrin presented a review on work performed in his own group, as well as by others, on the role of inflammation and immunity in hypertension. Ziad Mallat followed similar lines in his presentation on signal transducers and activators of transcription 3 signaling in atherosclerosis and aneurysm. Together, these 2 lectures represented an important paradigm shift in vascular research. Molecular mechanisms lead to vascular phenotypes, which constitute the basis for different risk factors for cardiovascular disease. Patrick Segers took the systems biology approach one step further in a mathematical model based study in apolipoprotein E1 mice in which he assessed the role of fluid mechanical factors in the development of abdominal aortic aneurysm. Two clinical-based presentations focused on metabolic mechanisms of altered arterial structure and function. Emmanuelle Lurbe discussed how BP and obesity exert independent influences on pulse wave velocity in youth. Isabel Ferreira showed that metabolic syndrome is associated with maladaptive carotid remodeling and stiffening.

In the session on microcirculation, Harry Struijker-Boudier presented a review on retinal microvascular phenotypes and genotypes. Adam Greenstein reviewed the role of the microcirculation in the cardiovascular risk associated with obesity. He focused on the role of adipose tissue and the vasoactive substances derived from that tissue. The next 2 presentations dealt with pre-eclampsia. Asif Ahmed provided evidence for a potential role of the anti-inflammatory enzyme...
heme oxygenase 1 and its metabolite carbon monoxide in the pathogenesis of eclampsia. Joey Granger reviewed the role of maternal endothelial dysfunction and, in particular, endothelin 1 in eclampsia.

The next session was devoted to pulse wave velocity as a biomarker for cardiovascular risk. In their guideline for assessment of cardiovascular risk in asymptomatic adults, the American College of Cardiology Foundation/American Heart Association task force stated that, “measures of arterial stiffness outside of research settings are not recommended for cardiovascular risk assessment in asymptomatic adults.” Such measures were qualified as class III, which means that no benefit is documented. However, numerous prospective studies have shown that aortic stiffness assessed as carotid-femoral pulse wave velocity was an independent predictor of cardiovascular prognosis in various populations. Furthermore, some studies have shown an incremental value of aortic stiffness, in terms of cardiovascular risk prediction, over and above conventional cardiovascular risk factors, helping reclassification of patients. Indeed, such statements could appear as antagonists, but before recommending measuring carotid-femoral pulse wave velocity in clinical practice, in addition to standard measurements, it seems wise to be convinced of its added value in terms of cardiovascular risk reduction strategies. One of the issues discussed during the workshop concerned the better parameter to deal with; it seems obvious that carotid-femoral pulse wave velocity is the gold standard in terms of aortic stiffness measurements, but aortic stiffness is correlated with other hemodynamic parameters. Which of these parameters would be the best biomarker candidate in the objective of optimizing risk reduction strategies? Central pulse pressure could act as a serious competitor. In the elderly, BP seems no more related to prognosis, and perhaps that aortic pulse wave velocity could lose its predictive value as well. Convincing data relating pulse pressure amplification and all-cause mortality were discussed, and BP amplification could also act as a serious competitor.

Then, in the absence of demonstration of a clear reversibility, central hemodynamic measures will probably continue to be confined to medical research. The designs of needed clinical trials have been extensively discussed. Ideally, an arterial stiffness–driven therapeutic strategy, aiming to normalize arterial stiffness in addition of normalizing “only” conventional cardiovascular risk factors, should be demonstrated as superior compared with a conventional strategy. However, methodological problems occur when we realize that most, if not all, drugs acting on arterial stiffness are antihypertensives; the arterial stiffness–driven therapeutic strategy could then be considered as “only” more intensive antihypertensive treatment, and, even positive, the conclusion of such a trial could be distorted and biased. The articles by Laurent et al. and Vlachopoulos et al. in this issue of Hypertension reflect the discussion during the workshop.

The last session of the workshop was devoted to BP variability. BP variability is a result of both heart rate and systemic resistance variability. The latter received much less attention because it is not easy to determine the instantaneous, beat-to-beat, systemic resistance. Berend Westerhof investigated the determinants of cardiac and peripheral variability and suggested that the baroreflex sensitivity assessed from heart rate or peripheral resistance values was weakly correlated and can be used to differently assess the autonomic function in patients. In the same line, Gianfranco Parati showed that aortic stiffness is strongly and independently correlated with the baroreflex sensitivity and, thus, with BP variability (BPV). Piotr Jankowski presented a new technique allowing assessment of central BP monitoring and then aortic pressure variability.

Yvonnick Bézie presented data evidencing that intermittent treatment of spontaneously hypertensive rats with valsartan (1 day over 3 days for 8 weeks) was able to normalize the BP values to the same extent that continuous (1 dose every day) treatment but did not prevent cardiac and vascular remodeling, thus suggesting a major role for BP variability. In contrast, Jacques Blacher analyzed BPV in a secondary cardiovascular prevention population (2501 patients) and showed that age, BP, and diabetes mellitus were the major determinants of BPV. However, the addition of BPV in models of prediction of major cardiovascular events did not markedly improve the prediction, suggesting that BPV could act more as an integrator of other cardiovascular risk factors than as a real independent factor.

Finally, Giuseppe Mancia pointed out the unknown aspects of BPV, such as the derivative of BP changes aiming to differentiate long, middle, and short time variability within months, days, or hours. Actually, these different BPV must be defined, the conditions and techniques of measurement precisely defined and validated, and, finally, their respective prognostic values investigated.

Thus, this session has evidenced 3 major points: (1) the pathophysiology of BP variability is now better understood; (2) its importance and reliability as a major and early marker of cardiovascular events in population studies remain to be further investigated; and (3) the duration of the measurement of BP variability, currently 24 hours, needs much more reflection and prospective studies.

Determinants of BPV vary from one study to the other and, from a practical practitioner point of view, the key question remains the evaluation of a potential additive value of BP variability in terms of strategy of cardiovascular risk assessment. Furthermore, in case of a significant additive value, the place of BPV in risk-reduction strategies should be further explored.

In this issue of Hypertension, you can read a selection of articles that were presented during the workshop. As organizers, we are most grateful to Servier for the unrestricted educational support for the workshop and the publication of its proceedings.

Disclosures

None.

References


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Hypertension. 2012;60:504-506; originally published online June 25, 2012;
doi: 10.1161/HYPERTENSIONAHA.112.198150
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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