The Emergence of Ambulatory Measurement of Arterial Stiffness and Central Blood Pressure. A Promising Novelty of Clinical Importance or Just Another Marker?

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Abstract: Whereas brachial blood pressure (BP) is still considered the gold standard for the estimation of cardiovascular risk in all clinical trials and guidelines, scientific interest is shifting towards central hemodynamics and the scientific community is experiencing a whole new revolution with the emergence of novel cardiovascular markers such as the ambulatory measurement of central BP and arterial stiffness. Central BP has already started to demonstrate its superiority over peripheral BP as a better and more reliable predictor of end-organ damage in cardiovascular diseases. Furthermore, ambulatory measurement of central BP and pulse wave velocity are expected to add much more useful information towards a more integrated assessment of cardiovascular risk and profile. However, more research is required before these novel markers could be incorporated in the everyday practice of BP measurement.

Keywords: Ambulatory monitoring, arterial stiffness, cardiovascular risk, central blood pressure, pulse wave velocity.

INTRODUCTION

Cardiovascular disease is the leading cause of death worldwide and hypertension is a major risk factor. Although cardiovascular medicine has presented novelties in the therapeutic field, brachial blood pressure (BP) is still considered the gold standard for screening, diagnosis and management of arterial hypertension and peripheral BP is still used as a major determinant of cardiovascular risk in clinical trials.

However, in the recent years central hemodynamics, namely central Systolic (cSBP) and Diastolic blood pressure (cDBP), pulse pressure (PP) and measurement of arterial stiffness, have emerged as novel parameters of cardiovascular risk in all clinical trials and guidelines, scientific interest is shifting towards central hemodynamics and the scientific community is experiencing a whole new revolution with the emergence of novel cardiovascular markers such as the ambulatory measurement of central BP and arterial stiffness. Central BP has already started to demonstrate its superiority over peripheral BP as a better and more reliable predictor of end-organ damage in cardiovascular diseases. Furthermore, ambulatory measurement of central BP and pulse wave velocity are expected to add much more useful information towards a more integrated assessment of cardiovascular risk and profile. However, more research is required before these novel markers could be incorporated in the everyday practice of BP measurement.

PATHOPHYSIOLOGY AND MEASUREMENT OF ARTERIAL STIFFNESS

Arterial stiffness describes a non-compliant artery that is a vessel unable to distend in response to different pressure changes. The two major determinants of arterial stiffness are arterial hypertension and aging. Their etiologic relationship resides in the structural and functional alterations that they provoke to the arterial wall, including smooth muscle hypertrophy, increased collagen deposition, degradation of elastic fibers and endothelial dysfunction [1-5].

The pathophysiological substrate of arterial stiffness lies on the velocity with which pulse wave travels along the arterial tree and the interrelationship between the incident and the reflected wave of the pressure waveform. Every time the heart beats a systole, an incident pulse wave generates at the junction with the aorta and propagates along the arterial tree. Propagation continues unimpeded until the pulse wave meets areas of discontinuity of the arterial wall, mainly the high resistance arterioles, thus generating a reflected wave [6]. In normal, healthy and young individuals where arteries are elastic and compliant, the reflected wave travels back towards the aorta and meets the oncoming incident wave during the early diastole thereby increasing diastolic pressure and facilitating coronary perfusion. However, in adults older than 50 years old and in elderly people, where aging and hypertension progressively stiffen the arteries, a different pattern of circulation exists. The incident wave is reflected in a much earlier point of the arterial tree and its reflected waveform travels much faster along the hardened arterial wall in a way that coincides with the oncoming incident wave during systole. The net result is augmentation of the cSBP and reduction of the diastolic pressure compromising the perfusion of the coronary arteries. At the same time, systolic hypertension increases the afterload of the heart thereby producing left ventricular hypertrophy and in the long term, heart dysfunction [7-12]. Furthermore, increased arterial stiffness is associated with progressive microvascular damage which compromises renal and cerebral function [13, 14].

The velocity at which the pulse wave travels along the arterial tree is the most direct marker of arterial stiffness and has been established as the gold standard for its measurement. The most common technique consists of measuring the
distance that a pulse wave covers between two steady body points (carotid and femoral artery) divided by the time needed to reach these sites under simultaneous electrocardiographic monitoring [15]. The selected arteries provide the advantage of a superficial, easy to access location whereas in-between them, lies almost the whole of the aorta which is the major vessel subject to arterial stiffening. In that Sense, pulse wave velocity (PWV) is a simple, non-invasive, reproducible technique and several lines of evidence have proved its significance as an independent prognostic factor of cardiovascular morbidity and mortality in patients with hypertension, diabetes mellitus type II, end-stage renal disease as well as in the general population [16-25]. The aforementioned value has established PWV as a marker of subclinical organ damage according to the latest guidelines of the European Society of Hypertension and European Society of Cardiology [26].

Despite the important relationship of arterial stiffness and PWV with significant hemodynamic components of the central arteries, paradoxically little research had been done so far in the field of cBP parameters.

FROM PERIPHERAL TO CENTRAL BP

Peripheral BP measurement has for long been and still is the established technique for evaluating arterial hypertension and cardiovascular risk, although we know that differences between peripheral and cBP exist.

In young healthy subjects cBP is lower compared to peripheral BP due to a physiological phenomenon called PP amplification. At this age, PP travels from the central, elastic arteries towards the smaller, muscular and more resistant arteries of the periphery thereby undergoing an augmentation of its amplitude. As a result, brachial BP can be as high as 30mmHg more compared to cBP. On the other hand, by aging the opposite effect is observed. Central arteries become stiffer and cSBP increases at a level higher than that of the periphery due to the magnitude of the reflected waves arriving at the heart. In addition, cBP represents more closely and more realistically the true load of the left ventricle because of its proximity to the key organs, including the heart [11, 27-32]. Taking these two factors into account, someone can conclude that the measurement of brachial BP in an elderly individual may not represent the true “hypertensive” load and his total cardiovascular risk because the central burden that strains his heart may be even larger.

The notion that cBP represents the true load of the heart pump and consequently the real cardiovascular risk, has been the epicenter of interest of a growing number of trials. As a matter of fact, much research has focused lately on demonstrating whether central arterial pressure could turn out to be a better marker of target organ damage and whether it could provide more reliable information regarding cardiovascular risk assessment. The first studies to be conducted, included patients with end-stage renal disease and indeed, underlined the role of cBP parameters in predicting all-cause mortality [33-35]. Since then, accumulating scientific evidence has proved that cBP can predict better cardiovascular events and can actually be an independent factor of cardiovascular morbidity and mortality [36-43]. Furthermore, it has been shown that different anti-hypertensive drugs may exert similar impact on peripheral BP whereas on the other hand, achieve different levels of cBP reduction [44-51]. Interestingly, various reductions in cBP resulted in different cardiovascular outcomes, an observation that further highlights the role of cBP as a better marker of target organ damage and cardiovascular risk [42, 45, 52].

Since accumulating evidence points towards a greater necessity for assessing the central hemodynamics, newer, non-invasive techniques for approaching these phenomena have emerged. Apart from piezo-electronic techniques (Compilior) and tonometric methods (Sphygmocor), the recent advent of oscillometric devices (Arteriograph, Mobil-o-graph) has offered the opportunity to measure peripheral and cBP parameters, including 24h monitoring of their variability [53, 54].

SIGNIFICANCE OF 24H AMBULATORY MEASUREMENT OF ARTERIAL STIFFNESS AND CENTRAL BLOOD PRESSURE

Although research in cardiovascular field has started to demonstrate the superiority of central over peripheral BP, there are characteristics not fully investigated yet, including cBP and PWV variability. In this context, since peripheral BP levels present a circadian rhythm during the day, it seemed reasonable that a similar pattern for cBP and PWV could exist. However, almost all trials conducted so far included BP measurements at resting conditions whereas variability of PWV has never been studied before.

The study by Luzardo et al. was one of the first attempts to assess ambulatory cBP and arterial stiffness parameters. The investigators enrolled 115 volunteers between 28 and 64 years old from their working environment. Although they were not a representative sample of the general population, the volunteers underwent tonometric and oscillometric measurements of arterial stiffness and cBP parameters under resting and ambulatory conditions. Measurements were performed using the validated Sphygmocor and Mobil-O-graph devices. Despite slight differences between cPP and PWV values among the two methods, the investigators proved that ambulatory, non-invasive measurement of cBP is a feasible procedure. Nevertheless, the study focused on comparing the values recorded between a tonometric and an oscillometric device and did not correlate possible diurnal changes of cBP to the established changes of peripheral BP. In addition, the ambulatory measurement of cBP did not include early morning and late night measurements, two time periods where the most important pathophysiologic alterations in peripheral BP take place [55].

More recently, Williams and his colleagues conducted the first multicenter, randomized, controlled, clinical trial in order to assess the 24h circadian profile of cBP. In addition, the investigators have been the pioneers in comparing, simultaneously, ambulatory cBP changes with the diurnal variation of peripheral BP. For the purposes of the study, the investigators enrolled 171 men and women with a mean age of 53 years old and a history of EH. After a wash-out period, participants were randomized into two treatment groups receiving either a direct renin inhibitor or an angiotensin receptor blocker. At the beginning and at the end of the study, ambulatory peripheral BP and cBP parameters were meas-
ured using a conventional, cuff-based, oscillometric device (Spacelabs) and a tonometric ambulatory BP monitoring device (BPro) at the same time. The study demonstrated that cBP changes throughout the day exhibit a similar pattern of variability just like the diurnal fluctuation of brachial BP. The observed diurnal pattern of both central and peripheral pressure remained the same even after administration of BP lowering agents suggesting that BP reduction does not play a role in between pressure’s inter-variability. However, of major interest was the observation that cBP levels remained lower than those of peripheral pressure for the whole 24h period whereas, and more significantly, exhibited a lower nocturnal dipping pattern compared to that of brachial pressure [56]. Whether this phenomenon is just a normal consequence of sleep or whether there are other implicating factors remains unknown and needs further investigation due to its apparent major clinical importance. Given the fact that the incidence of cardiovascular events is higher in non-dipper hypertensive individuals [26], someone could conclude that variations of BP during postural movements could negatively affect the precise measurement of arterial stiffness parameters. The observed obstacle is one of the reasons why efforts to obtain ambulatory PWV measurements are still confined to a very rudimental, experimental level [57, 58]. In this context, until more reliable methods for the ambulatory measurement of PWV come up, diurnal variation of arterial stiffness and its possible applications - implications will continue to be a promising field of cardiovascular research.

CONCLUSIONS

Whereas peripheral BP continues to be the point of reference of all algorithms and guidelines regarding arterial hypertension and cardiovascular risk, it seems reasonable that in the very near future measurement of cBP will play a major role in cardiovascular risk stratification and treatment. Mounting evidence from large-scale trials has demonstrated the significance of cBP as a better marker of target organ damage and consequently as a more reliable predictor of cardiovascular morbidity and mortality. In addition, it has been demonstrated that antihypertensive treatment can provoke different changes in cBP parameters consequently changing cardiovascular outcomes. These observations could revolutionize our therapeutic strategies making arterial stiffness and cBP the primary therapeutic targets.

However, more research is needed before applying cBP parameters into every day clinical practice. The advent of ambulatory monitoring of cBP and probably, in the long term of arterial stiffness, will be a determining factor in the effort to understand the masked properties of central hemodynamic components. With only a few trials published so far, it is undoubtedly a virgin field for future cardiovascular novelties.

CONFLICT OF INTEREST

The author(s) confirm that this article content has no conflicts of interest.

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