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Applanation Tonometry; an Innovative Diagnostic Tool for Central Aortic Pressure: A Review

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ABSTRACT

Blood pressure when measured with a sphygmomanometer in the brachial artery is an important predictor of cardiovascular risk assessment. A person's systolic pressure varies throughout the arterial wall, so that (central) systolic pressure is lower than the brachial pressure, and also these pressures are highly different in individuals. Now, most of the clinical study suggests that central pressure is better related to future cardiovascular events than brachial pressure. So anti-hypertensive drugs can exert differential effects on brachial and central pressure. Therefore, starting treatments on central pressures diagnosing by applanation tonometry, rather than brachial pressure, is likely to have important interventions for the future diagnosis and management of hypertension. Hence targeting central pressure, brings added benefit, over and above that already provided by brachial artery pressure.

INTRODUCTION

Cardiovascular diseases (CVDs) are disorders that include several heart diseases of the circulatory system. The World Health Organization refers the CVDs as the worldwide leading cause of death, resulting in several annually deceased people higher than from any other cause. The improvements in diagnostics, treatments, medications, and surgical techniques were responsible for a significant decrease in total CVD mortality over the past few decades[1]. Recently, many studies have indicated that arterial stiffness is an independent predictor of increased morbidity and mortality for Cardiovascular Diseases (CVD) such as atherosclerosis in general, and coronary artery disease, peripheral artery disease, chronic kidney disease, hypertension, cerebral stroke, in particular[2-11].

Epidemiological studies have shown that damage to large arterial vessels is a major risk factor to the high cardiovascular morbidity and mortality of end-stage renal disease (ESRD) patients. The macrovascular disease develops in uremic patients and is responsible for the high incidence of ischemic heart disease, left ventricular dysfunction, congestive heart failure, death, and stroke. The most common causes of arterial stiffening are increased central blood pressure due to higher systolic blood pressure (SBP) and lower diastolic blood pressure (DBP)[12].

The assessment of changes in the cardiovascular system and the identification of risk factors is of greater importance to avoid hospitalization and to reduce CVD morbidity and mortality rates. The early detection is based on several parameters of pathological conditions which are the key to patient survival. Current CV risk assessments are based on clinical judgment and traditional methods, including heart rate, respiratory rate, blood pressure (BP), temperature and pulse oximetry. However, these vital signals are not sufficient to predict and evaluate the CVDs risk, so with new biomarkers such as pulse wave velocity (PWV), augmentation index may represent a better method for more accurate diagnosis[13].

Biomarkers are characteristics that are measured and evaluated as indicators of normal stages or pathogenic processes and responses to therapeutic interventions. Efforts to identify new biomarkers have largely focused on the use of new measurements. PWV is an emerging biomarker useful for CV risk stratification of patients, assessment of BP, vascular stiffness and therapeutic effects and efficacy in clinical studies. The arterial stiffness is the first sign which is responsible for several risks, which can lead to CVDs. For this reason, the arterial

elastic properties are used for risk stratification purposes in several populations. The guidelines given by the European society of cardiology in the management of arterial pressure suggested the measurement of Pulse wave velocity is considered the gold standard method for assessing arterial stiffness[13].

NON INVASIVE MEASUREMENT OF CENTRAL BLOOD PRESSURE:

Central pressures can be derived from noninvasive techniques by measuring radial and carotid pulses[14]. These involve applanation tonometry in which transcutaneous pressure transduces at the end of a probe obtain pressure waveforms that are almost identical to those obtained using intraarterial measurement. It can be used for radial, carotid and femoral arteries. By using this method we can measure central systolic BP, diastolic BP, pulse pressure. Indices of arterial stiffness such as augmentation index and pulse wave velocity (PWV) are estimated. The applanation tonometry is more accurate and standard than conventional brachial cuff pressure with sphygmomanometer[15].

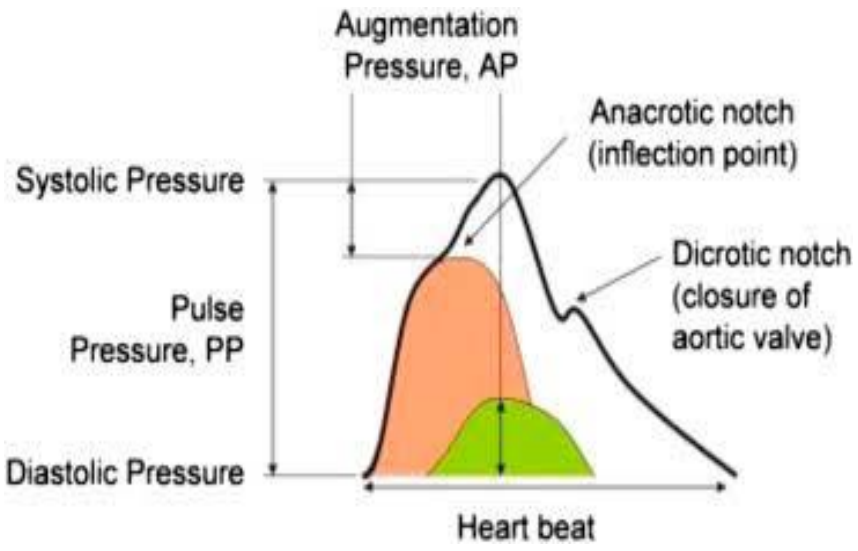

Figure No. 1: The augmentation index is a ratio calculated from the blood pressure waveform (augmentation index= ΔP/pulse pressure). It is a measure of the enhancement of the central aortic pressure by a reflected pulse wave (shown in green in the graph)

The pulse wave velocity is the measurement of aortic velocity which can be assessed by measuring the distance between the carotid and femoral arteries and dividing by the transit time. An increase in arterial stiffness means fewer complaint arteries. Pulse wave velocity is the better biomarker of arterial stiffness because of its ease of measurement. It is not influenced by smoking, dyslipidemia, or sex, but to some extent by heart rate and diabetes.

Pulse wave velocity is a strong predictor of future cardiovascular events and all-cause for mortality and morbidity[15].

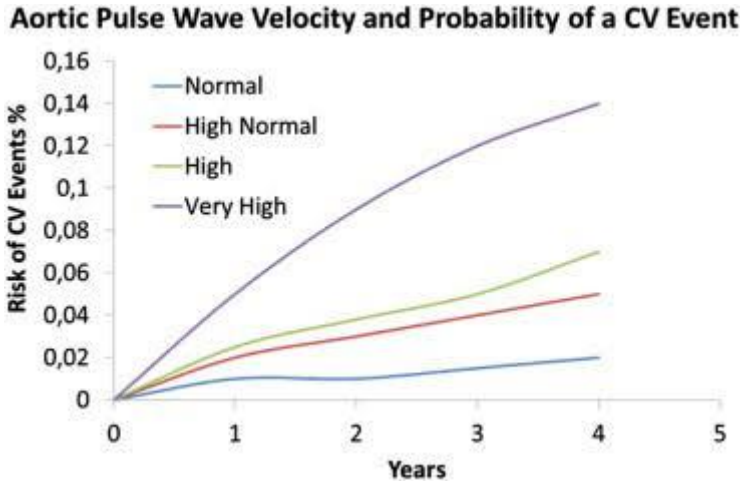

Figure No. 2: Pulse wave velocity and risk of a major cardiovascular event

METHOD FOR CENTRAL BLOOD PRESSURE MONITORING VIA A STANDARD AUTOMATIC ARM CUFF:

The developed method computes the central blood pressure waveform from a cuff pressure waveform obtained only during deflation or inflation by the successive application of three sub-methods. First, to yield brachial systolic and diastolic BP a patient-specific method is applied to an oscillogram (derived from the waveform). Next to extract a "deflation PVP" waveform and scale it to the brachial BP levels and a calibration method is applied to the variable amplitude cuff pressure oscillation waveform (obtained by high pass filtering the cuff pressure waveform). Finally, a variable transfer function (VTF) method is applied to convert the brachial BP-like waveform to the central blood pressure waveform. In an Indian scenario mainly for the diagnosis and treatment of hypertension is purely based on brachial blood pressure, but many studies have shown that brachial and central blood pressures are not the same. A study by Bilal Ahmad Baba et al on an Indian population clearly showed that central aortic pressure measurement is having a greater significance than the brachial pressure[16].

Figure No. 3: Applanation tonometry

Figure No. 4: Conventional brachial pressure measurement

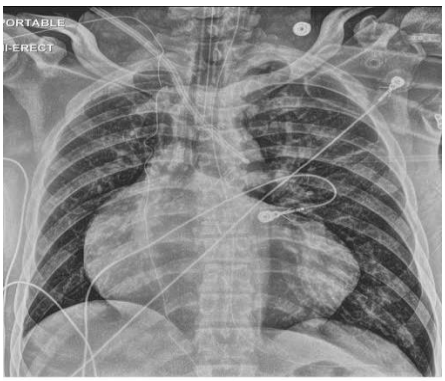

Figure No. 5: Invasive cardiac catheterization

IMPLICATIONS FOR THERAPY

The evidence shows that some antihypertensive drugs may provide target organ protection beyond their effect to decrease brachial BP. Large multicentre trials comparing 2 active treatments including the Second Australian National Blood Pressure (ANBP2) study[21], Losartan Intervention For End Point Reduction in Hypertension (LIFE)[22], Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT)[23]and Avoiding Cardiovascular Events

Through Combination Therapy in Patients Living With Systolic Hypertension (ACCOMPLISH) [24]have shown clinical benefits of BP-reducing strategies including a calcium channel blocker or a renin-angiotensin blocker (an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker) that were superior to treatments based on a b-blocker (BB) or a Thiazide diuretic for approximately the same level of peripheral (brachial) BP. The brachial BP control could be explained by a neutral metabolic effect of some antihypertensive agents with better tolerability, and thus can improve adherence. The vascular protective effect on appropriate organs or surrogate risk predictors such as arterial stiffness or central BP could be also related to reduced CV morbidity or mortality. Effects on central pressures will not possible according to pressure measurements of a peripheral (brachial) artery since the resultant wave is added to a different part of the central waveform (ie, AIx)[25]. This is one of the reasons why drugs that provide a similar reduction in peripheral pressures have a different effect on CV outcome.

The largest randomized controlled trial was conducted to test the hypothesis of the clinical significance of decreased central pressures was the Conduit Artery Function Evaluation (CAFE) study which is a substudy of the ASCOT study. In the ascot study, a total of 2199 patients were enrolled for detecting central aortic pressures and hemodynamic indices using radial artery applanation tonometry and pulse wave analysis. Comparing atenolol based regimen with Amlodipine based regimen within similar treatment groups, much larger reductions were seen in the group using Amlodipine based regimen in the central aortic systolic blood pressure and central aortic systolic pulse pressure. This greater reduction in central pressures was associated with a significantly greater reduction in CV events and the development of renal impairment. Central BP might be a very useful index for CV risk assessment, it has not yet been tested in a randomized controlled trial with clinical endpoints and treatment guided by a central BP goal or arterial stiffness markers[26]. Recent studies shown that using central BP, to guide the choice of antihypertensive therapy leads to the use of less medication compared with the control group of usual care in measuring arm BP.

PHARMACOLOGICAL REDUCTION OF CENTRAL AORTIC PRESSURE:

Thiazide diuretics generally do not affect pulse wave velocity (PWV) and arterial wave reflection[17]. Some beta-blockers have a favorable effect on arterial stiffness which is measured according to a decrease in PWV or wave reflection, but not consistently Atenolol and metoprolol did not affect PWV. When comparing atenolol and metoprolol, the peripheral

BP reduction was the same, but the augmentation index (AIx) was increased [18-20]. Bisoprolol reduced PWV in only some arterial areas studied and nebivolol consistently improved PWV and AIx. Carvedilol has improved all central BP parameters but not as well as losartan for the AIx. Calcium channel blockers, specifical dihydropyridines, reduce PWV and wave reflection, but amlodipine has not been studied; data are limited for now dihydropyridines[17]. Renin-angiotensin blockers (angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists) induce vasodilation, reverse vascular hypertrophy, and increase arterial compliance. They all reduce the pulse wave velocity and wave reflection. It is unclear what other medications with vasodilatory effects (ie, clonidine, a-blockers, and hydralazine) can improve central BP components.

Table No. 1: Effects of hypertension medications on wave reflection and PWV

Antihypertensive class	Augmentation index (Alx)	Pulse wave velocity(PWV)
Diuretics	No Change	No Change
Calcium channel blockers (dihydropyridines)	Improvement	Improvement
Angiotensin-converting enzyme inhibitors	Improvement	Improvement
Angiotensin-receptor antagonist	Improvement	Improvement

Table No. 2: Effects of beta-blockers on wave reflection and PWV

Beta-blockers	Augmentation index (Alx)	Pulse wave velocity (PWV)
Propranolol	No Change	No Change
Atenolol	No Change	Improvement
Metoprolol	Possible improvement	No Change
Labetalol	Improvement	Improvement
Carvedilol	Improvement	Improvement
Nebivolol	Improvement	Improvement

CONCLUSION

The non-invasive method using applanation tonometry appears to be reasonable by transforming pulse wave velocity and brachial blood pressure into aortic pressure values. The results obtained by applanation tonometry and oscillometric pulse wave velocity show that the latter can be used non invasively to find out the aortic pressure in patients However, more studies should be done in a larger population. Cuff measurements of brachial systolic and diastolic pressure continue to remain the accepted surrogates by drug regulatory authorities. This means that new therapies will continue to be assessed based on central pressure measurements, which may ultimately serve as a new strategy for the reduction of blood pressure. Therefore, lowering of central pressure improves outcome, will ultimately be required before central pressure becomes an accepted surrogate of cardiovascular risk.

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