

Aortic Pulse Wave Velocity, an Independent Marker of Cardiovascular Risk

Summary

H. Safar, J.-J. Mourad, M. Safar
and J. Blacher*

Aortic pulse wave velocity (PWV), a classical index of aortic stiffness, may be easily measured in humans using non invasive ultrasound methods of high reproducibility. Recent epidemiological studies have shown that, independently of confounding factors as age, blood pressure and cardiac mass, aortic PWV is a predictor of cardiovascular (CV) mortality in populations of hypertensive subjects, whether they have or not end-stage renal disease.

Since aortic PWV is dominantly influenced by age, this finding may be of major importance for the evaluation of CV risk in geriatric populations. Arch Mal Cœur 2002 ; 95 : 1215-8.

Résumé

La vitesse de l'onde de pouls aortique (VOP) est une mesure classique de la rigidité artérielle, facilement utilisable chez l'homme par mesure non invasive ultrasonique. De récentes études épidémiologiques ont montré que la VOP est un prédicteur indépendant de la mortalité cardio-vasculaire chez les sujets hypertendus, qu'ils aient ou non une insuffisance rénale.

Comme la VOP est influencée de manière importante par l'âge, ce résultat épidémiologique est particulièrement important à considérer dans les populations gériatriques à haut risque cardio-vasculaire. Arch Mal Cœur 2002 ; 95 : 1215-8.

(*) Department of Internal Medicine and Inserm U541, Broussais Hospital, Paris.

e-mail : michel.safar@brs.ap-hop-paris.fr

(Tirés à part : Dr H. Safar).

Large artery damage is a major contributor to cardiovascular diseases and therefore requires an early evaluation in the general context of cardiovascular (CV) risk factors. Several methods have been proposed to analyze the structure and function of large arteries [1]. Most of them are complex or need sophisticated technical equipment which limits their application in clinical practice. Among the noninvasive and simple methods of evaluating arteries, pulse wave velocity

(PWV) measurement is widely used as an index of large artery elasticity and stiffness [2]. This method is simple, accurate and, reproducible and thus can easily be applied for the evaluation of CV risk.

BASIC HEMODYNAMIC CONCEPTS

In the absence of widely used non invasive aortic blood pressure measurements [3], PWV may be an avail-

lable method to evaluate the status of central arteries. During systole, the contraction of left ventricular myocardium and the ejection of blood into the ascending aorta dilate acutely the aortic wall and generate a pulse wave which propagates along the arterial tree at a finite speed. This propagation velocity constitutes an index of arterial distensibility and stiffness: the higher the velocity, the higher the rigidity of the vascular wall and the lower the distensibility [3].

The pressure pulse generated by ventricular ejection is propagated throughout the arterial tree at a speed which is determined by the elastic and geometric properties of the arterial wall and the characteristics (density) of the contained fluid (blood). Since blood is an incompressible fluid and is contained in elastic conduits (arteries), the energy propagation occurs predominantly along the walls of the arteries and not through the incompressible blood. Thus, the properties of the arterial wall, its thickness, and the arterial lumen diameter are the major factors influencing PWV. The relationships between PWV, transmural pressure, wall tension and distensibility have been formalized in many mathematical models. In most of them, the arterial segment studied is considered as a tube either with a thin or a thick vascular wall. Inside this cylindrical tube, there is a positive relationship between the change in pressure and the change in volume (V). The latter is usually expressed per unit length and then evaluated in terms of changes in diameter or radius, considering the length of the tube as constant. In that conditions, PWV may be defined according to the Moens-Korteweg and the Bramwell and Hill equations [3].

MEASUREMENT OF AORTIC PWV

PWV may be measured in various segments of the arterial circulation [3]. When two pressure waves are recorded at two different sites of the vascular tree, it is possible, owing to the propagation of the waves, to measure the time delay (Dt) and the distance D between these two waves. PWV is then defined as D/Dt. Measurement of time delay is usually performed by determination of a foot-to-foot transit time.

Since the aorta is the major component of arterial elasticity, the carotid-femoral PWV offers the most simple reproducible and noninvasive evaluation of regional stiffness. This measurement allows the recording of the pulse pressure at 2 different sites of the aorta and the measurement of the distance between the two pressure waves. The former is usually done at the site of the common carotid artery and the femoral artery, using standard blood pressure (or even velocity) transducers enabling an adequate recording, particularly of the foot of the pressure wave, and therefore, the calculation of the time delay between the carotid and the femoral waves. The latter is the non invasive measurement of the distance between the carotid and femoral recordings. It is important to recall that an accurate measurement of

this distance is obtained only with invasive procedures. In this regard, some authors suggested, for non invasive measurements, a possible correction based on anatomic dimensions of the body, whereas others recommended subtracting the distance between the suprasternal notch to the carotid location from the total distance when the carotid pulse pressure is recorded instead of the aortic arch pulse, because of the pulse traveling in the opposite direction. In clinical practice, arteries become longer and tortuous with age making that the path lengths determined from superficial linear measurements are underestimated. Repeatability studies, checks made with Bland and Altman diagrams, and modern computer technology now made aortic PWV quite feasible to simply investigate aortic stiffness in CV epidemiology [2].

In clinical studies, the principal factors modulating the level of PWV are age, blood pressure and to a lesser extent, gender. These parameters represent more than 50% of the variability of aortic PWV: the higher the age, the higher the pressure and the higher the aortic PWV. In epidemiological studies, in order that PWV reflects arterial stiffness independently of age and blood pressure, PWV should be adjusted to these 2 parameters. This approximation is true below 70 years of age. Above 70 years, aortic PWV is exclusively influenced by blood pressure, but not by age [4].

AORTIC PWV AS A MARKER OF CV RISK

In the recent years, epidemiological investigations have been performed in hypertensive subjects in the presence or absence of end-stage renal disease (ESRD).

In a cohort of 241 subjects with ESRD with an average follow-up of 11 years [5], logistic regression and Cox analysis identified two dominant predictors of CV and all cause mortality: PWV, and age at inclusion. Hemoglobin and low diastolic blood pressure (DBP) were also predictive but to a much smaller extent. After adjustment for confounding variable including in particular age, left ventricular hypertrophy, and blood pressure, the odds ratio for PWV (>12.00 m/s vs. <9.4) was 5.4 (95% confidence interval: 2.4-11.9) for all-cause mortality, and 5.9 (95% confidence interval: 2.3-15.5) for CV mortality. These results provided the first evidence that, in patients with ESRD undergoing hemodialysis, increased aortic stiffness is a major and independent predictor of CV and all cause mortality (fig. 1). Furthermore, in these patients with ESRD, similar results were obtained when carotid incremental elastic modulus was used in place of PWV as an index of the stiffness of carotid arterial wall material [6].

In subjects with essential hypertension, the situation is more complex because longitudinal studies on arterial stiffness as a CV risk factor are lacking. However, calculation of CV risk using Framingham

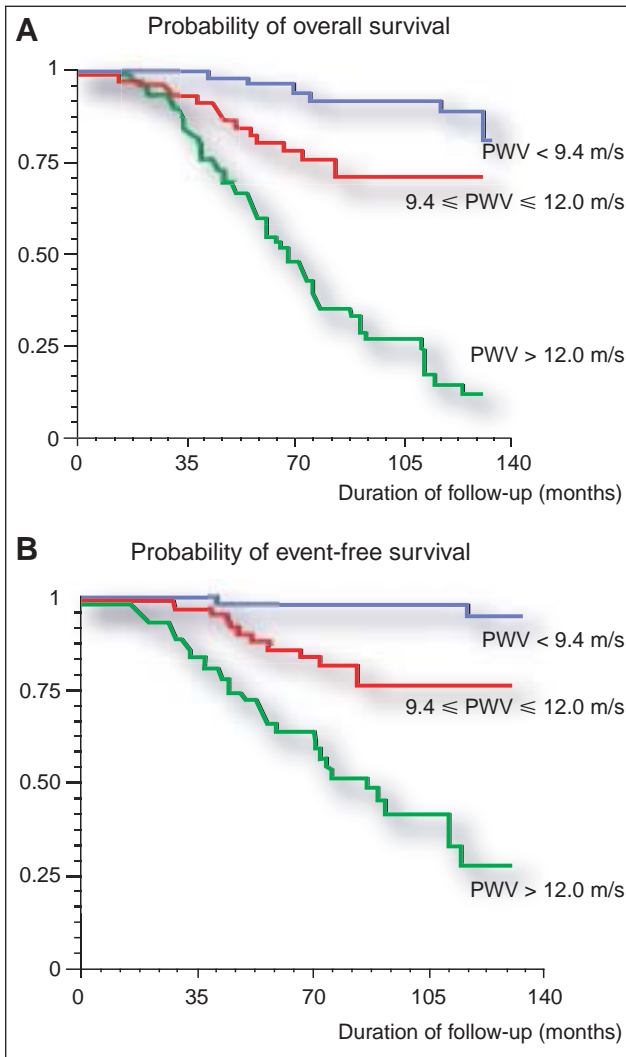


FIG. 1 – Probabilités de survie globale (A) et sans événement (mortalité cardiovasculaire, (B) dans la population de l'étude avec l'insuffisance rénale terminale divisée en 3 sous-groupes selon le niveau de la vitesse de l'onde de pouls. Comparaisons entre les courbes de survie étaient très significatives (khi square = 47,04 pour mortalité cardiovasculaire et 67,23 pour mortalité globale ; $p < 0,0001$ pour les deux) [5].

FIG. 1 – Probabilities of overall (A) and event-free survival (cardiovascular mortality, (B) in the study population with end stage renal disease according to the level of pulse wave velocity divided in tertiles. Comparisons between survival curves were highly significant (khi square=47.04 for cardiovascular mortality and 67.23 for overall mortality; $p < 0.0001$ for both) [5].

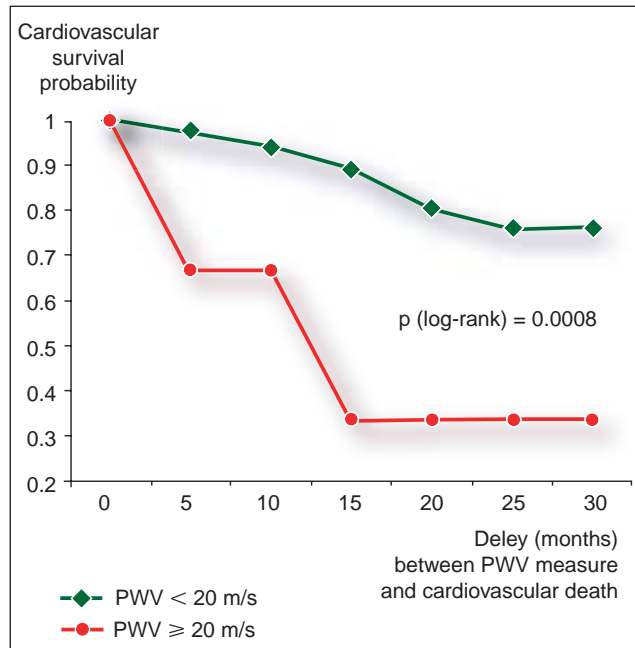


Fig. 2 – Sujets > 70 ans : survie CV en fonction de PWV [11].

Fig. 2 – Subjects >70 years of age: CV survival as function of PWV [11].

equations [7] can partially resolve this problem. This was done in a study including 710 subjects with hypertension, in which the odds ratio of being in a high-risk group based on the presence or absence of various CV risk factors was assessed [8]. The risk of any CV complication consistently increased in parallel with the increase of the single measurement of PWV. Furthermore, at any given value of age, aortic PWV was the best theoretical predictor of CV mortality and even more potent than age, blood pressure and cardiac mass. The odds ratio of being in the group at high risk of CV mortality (>5% for 10 years) for patients with $PWV > 13.5\text{ m/s}$ was 7.1 (95% confidence interval: 4.5-11.3). This study provided the first evidence that a single measurement of aortic PWV constitutes a potent indicator of CV risk in hypertensive patients. These findings are in agreement with recent longitudinal studies which showed that the ratio between stroke volume and PP, an indirect marker of arterial stiffness, and aortic PWV, a direct marker, were independent predictors of CV risk [9-11] (fig. 2, table).

TABLE - PWV IN ATHEROSCLEROTIC SUBJECTS AFTER ADJUSTMENT FOR AGE AND MAP: THE TABLE SHOWS THAT ATHEROSCLEROTIC ALTERATIONS WITH MULTIPLE SITES INVOLVE CONSTANTLY AN INCREASE OF PWV [12]

	PWV (m/s)	Age (years)	MAP (mmHg)	Adjusted PWV (m/s)
No site	12.8	59	103	13.8
Lower limb site	16.4	71	103	15.8
Aortic site	15.4	70	103	15.1
Lower limb and aortic sites	19.3	66	107	19.2

Values are means. PWV was significantly different between "no site" and the three other groups ($p = 0.001$; Scheffé test). MAP: mean arterial pressure; PWV: pulse wave velocity.

It is important to note that, in hypertensive subjects with or without ESRD, PWV was a predictor of CV risk independently of blood pressure level and/or cardiac hypertrophy. In all these studies, the Odds ratio were higher for PWV than for the two other parameters. When blood pressure and PWV were both involved in logistic regressions, it was constantly a low (and not a high) DBP which predicted CV risk [8, 13].

In summary, these findings suggest that increased aortic PWV is a strong independent predictor of CV risk, regardless of whether this mechanical factor

plays a causative role in CV risk or merely serve as a marker of vascular disease already present. Clearly the former hypothesis needs to be tested using specific intervention studies, as recently published [14].

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KEY WORDS : aortic pulse wave velocity, arterial stiffness, hypertension, elderly, end stage renal disease.

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