Blood Pressure Variability. Importance in Research and in Clinical Hypertension

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Since the pioneering observations of Stephen Hales in 1733, a number of papers have shown that blood pressure is not a constant parameter, but on the contrary, it shows high variability [1]. Only in the late sixties, however, it has been possible to obtain a detailed quantitative assessment of blood pressure variability, thanks to the development of a device for intra-arterial blood pressure monitoring in ambulant subjects (Oxford technique) [2,3], which has provided us with a quantification of both slow and fast changes in blood pressure all over the 24h.

Mechanisms and physiological implications - Several studies have investigated the mechanisms responsible for long and short term blood pressure fluctuations, and have provided clear evidence on the prominent role exerted in this context by neural factors, of either reflex or central origin [4-8]. These observations have lead to the suggestion that 24h blood pressure variability could be taken as a tool to evaluated some aspects of neural cardiovascular control. In particular, the detailed analysis of specific components of blood pressure and heart rate variability, carried out in the frequency domain by espectral analysis techniques applied to recordings obtained in standardized conditions, has been proposed as a means to assess the contribution of sympathetic and parasympathetic influences on cardiovascular regulation [9]. Moreover, the combined computer analysis of selected patterns in blood pressure and heart rate variability either in the time or in the frequency domain has been reported to yield a non-invasive and dynamic index of the baroreflex control of the heart (sequence analysis [10] and spectral analysis [11,12]).

Clinical implications - The assessment of 24h blood pressure variability is not only important as a research tool in investigating the pathophysiology of hypertension, but it may be also relevant in the clinical evaluation of hypertensive patients and in the assessment of the effects of antihypertensive treatment. Indeed, several studies have shown that the end-organ damage associated with hypertension is more closely related to the average 24h or daytime ambulatory blood pressure than to isolated blood pressure reading [13-15]. Not only the 24h blood pressure mean value, but also 24h blood pressure variability seems to be independently related to the end organ damage of hypertension. This is illustrated in figure 1, which is taken from a study where 108 hypertensive patients underwent a 24h intra-arterial blood pressure monitoring in ambulatory conditions by Oxford technique [16]. A score based on clinical and laboratory examinations was used to quantify the severity and the rate of end organ damage related to hypertension. The 108 patients were subdivided into five groups with progressively higher 24h mean blood pressure levels. In each group, the hypertensive patients with greater blood pressure variability (evaluated as the standard deviation of the 24h mean blood pressure) showed more severe and more frequent end organ damage than the patients with similar 24h mean values but less pronounced 24h blood pressure variability.

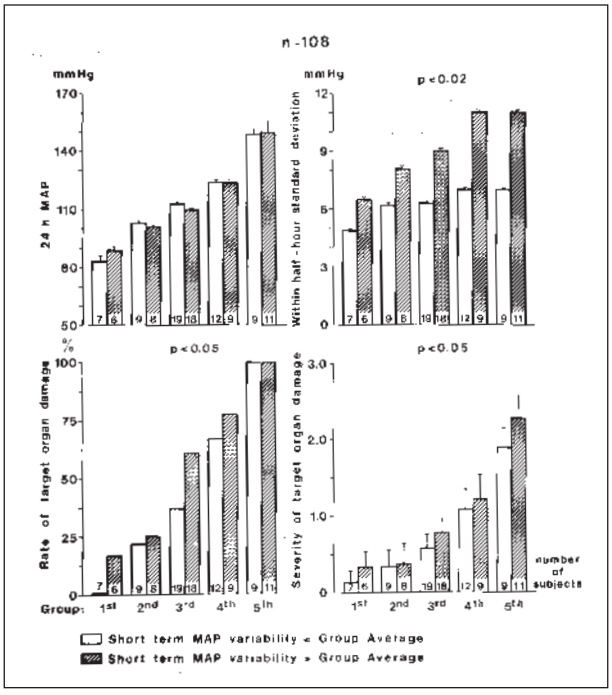

Fig. 1 - Rate and severity of target organ damage in 108 hypertensive patients. The patients were divided into five groups according to the increasing value of 24h average mean arterial pressure (MAP). The patients in each group were further subdivided into five classes according to whether their short-term variability expressed as within half hour standard deviation of MAP was below (open bars) or above (dashed bars) the average short-term variability of the group. Note that within each group classes had a similar 24h MAP but that the rate and the severity of target organ damage was less in the class in which blood pressure variability was lower. For each class, target organ damage is expressed as the percentage of subjects exhibiting the damage, and the severity of target organ damage is expressed as a subjects' average score based on data collected during laboratory and clinical examination. P- refers to the difference between all couples of classes (from Parati et al [16] by permission).

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Other papers by Pessina et al [17], Palatini et al [18] and Verdecchia et al [19] have later confirmed the possible clinical relevance of blood pressure variability in hypertension.

The importance of blood pressure variability in contributing to cardiovascular complications was also emphasized by other studies which showed: 1) a greater frequency of ischemic coronary events at the time of the morning increase in blood pressure [20]; 2) the occurence of a close relationship between the end-organ damage of hypertension and the blood pressure peaks occuring over the 24h [21], and 3) a significant relation between the cardiovascular complications of hypertension, and the increase in blood pressure occuring during stress or exercise [22].

Prognostic value? - An intriguing question still to be definitely answered is the possible predictive value of blood pressure variability. This topic has been addressed in a study by Frattola et al [23] in which after an initial clinical and laboratory evaluation, which included 24h ambulatory intra-arterial blood pressure monitoring, a group of 73 hypertensive patients were re-examined more than 7 years later. At comparable 24h mean blood pressure values at the initial evaluation, subjects with higher 24h blood pressure variability (24h standard deviation) displayed at the follow-up visit a greater severity of end-organ damage (assessed as an overall score or as increased left ventricular mass index at the echocardiographic examination - fig. 2). This may indicate that blood pressure variability represents an independent risk factor for future cardiovascular complications, a risk factor that, as shown in this study in which patients were under optimal drug therapy during the follow-up period, is not easily controlled by conventional antihypertensive treatment. Further controlled prospective studies are needed, however, to confirm these findings on larger database.

How to assess blood pressure variability non-invasively? - A major problem in the assessment of blood

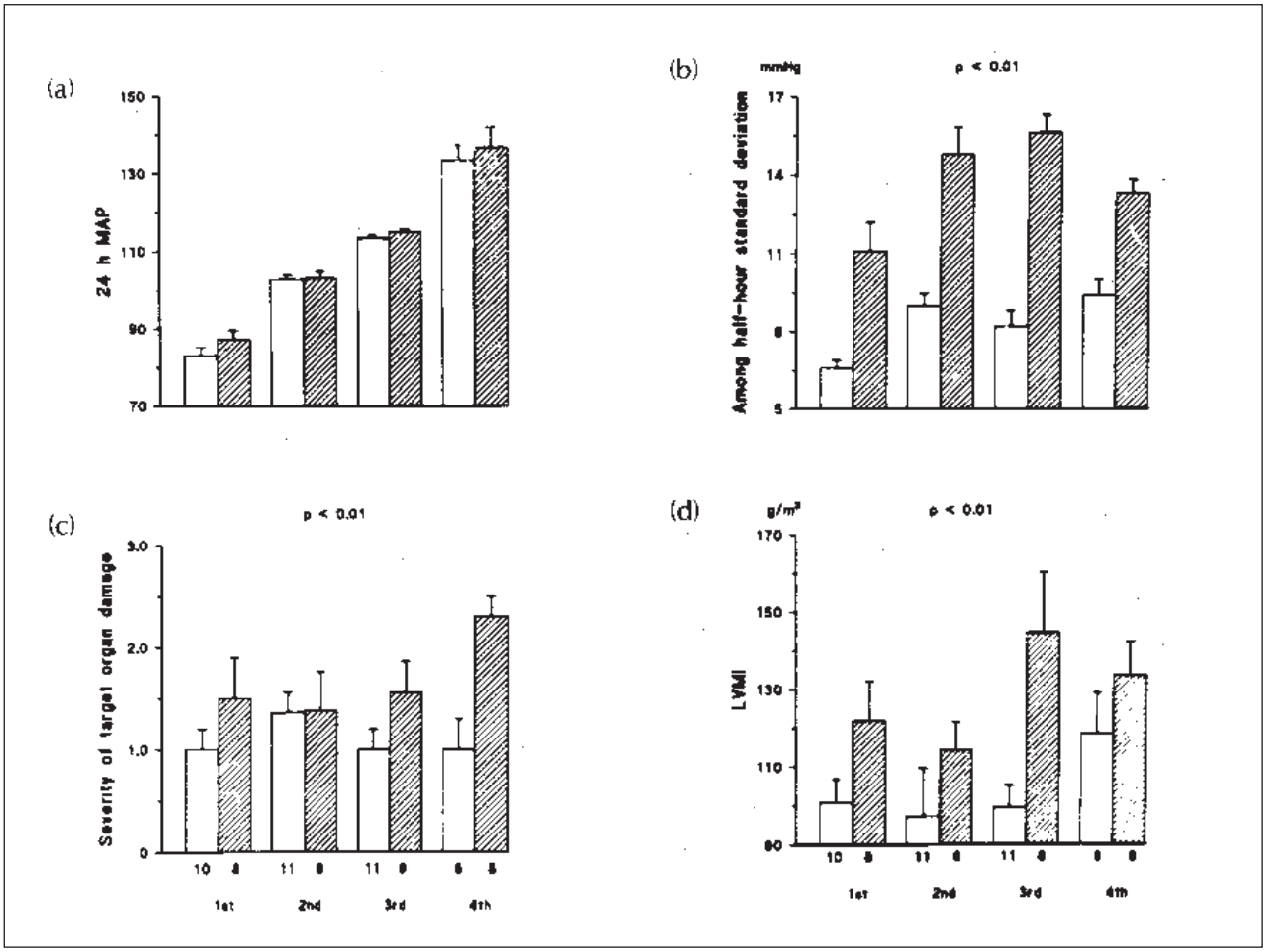

Fig. 2 - The severity of end organ damage and the degree of left ventricular mass index (LVMI) were assessed in 73 patients at a follow-up visit, after subdividing them into four groups according to their increasing levels of 24h mean intra-arterial blood pressure (MAP) values assessed by ambulatory intra-arterial monitoring on average 7 years before. The subjects in each group were subdivided into two classes according to whether the among half-hour SD of mean arterial pressure (long-term variability) was above (dashed bars) or below (open bars) the average long-term blood pressure variability for that group. Within each group the two classes had a similar 24h mean arterial pressure, but the severity of end organ damage and the left ventricular mass index were lower in the class in which long-term variability was lower (open bar). For each class the severity of end-organ damage was expressed as the average score for all subjects in that class. The number of subjects in each class is shown below each bar. P<0.01 refers to the difference between classes in all five groups (from Frattola et al[23], by permission).

pressure variability is that proper analysis of this phenomenon requires the availability of continuous blood pressure recordings. Until recently, this was possible only by means of the intra-arterial approach, a method which is characterized by well known disadvantages. In the last few years a new technique based on the principle of the vascular unloading and on the use of a photoplethysmografic-arterial/volume clamp method applied at the finger level, has offered us the possibility to monitor blood pressure non-invasively on a beat-to-beat basis [24,25]. This device (named finapres) is now available in a portable version (named portapres), developed in the TNO Laboratories of the University Hospital of Amsterdam. As shown in figure 3, finapres and portapres devices provide blood pressure values similar to those simultaneously obtained by means of intra-arterial catheter at rest, during application of laboratory manoeuvres and in ambulatory conditions, respectively [26-28], and seem also able to offer a reliable assessment of blood pressure variability.

Further progress in the implementation if these devices is likely to represent an important step forward towards the possibility of precisely quantifying 24h blood pressure fluctuations in ambulant subjects in different physiological and patophysiological conditions.

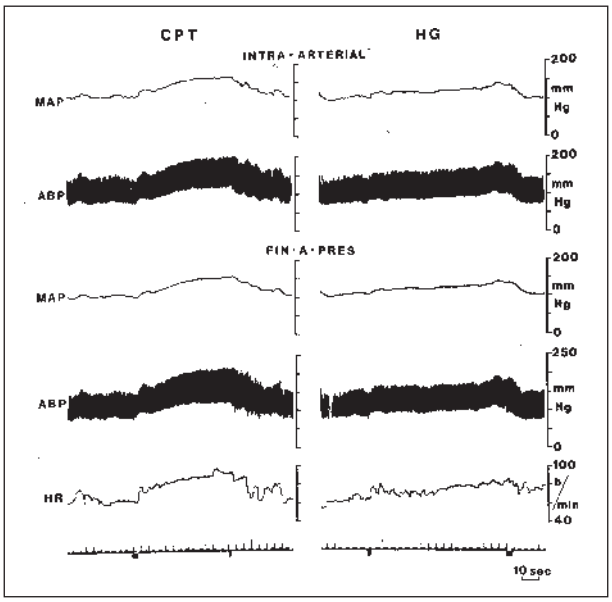

Fig. 3 - Original intra-arterial (upper panels) and finger blood pressure (finapres, lower panels) tracings obtained in one subjects during handgrip (HG) and cold pressure test (CPT). MAP- mean arterial pressure; ABP- pulsatile arterial blood pressure; HR- heart rate (from Parati et al [26], by permission).

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