

# Interpretation of Ambulatory Blood Pressure Profile: A Practical Approach for Clinicians

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Twenty-four-hour non-invasive ambulatory blood pressure (ABP) monitoring is increasingly used and recommended in subjects with clinical diagnosis of hypertension in order to refine prediction of cardiovascular (CV) risk related to BP [1-3].

A number of studies have suggested that the risk of hypertensive CV complications correlates more closely with ambulatory than with the office BP [4].

One of the first studies that addressed the prognostic value of ambulatory BP in hypertension was carried out by our group in 1994 [5]. We prospectively followed for up to 7.5 years, 1187 subjects with essential hypertension enrolled in the "Progetto Ipertensione Umbria Monitoraggio Ambulatoriale" (PIUMA) who had baseline off-therapy 24-hour noninvasive ABP monitoring. Our study demonstrated that ABP stratifies CV risk in essential hypertension independent of clinic BP and other traditional risk markers including echocardiographic left ventricular (LV) hypertrophy [5].

Twenty years after this landmark study, clinical usefulness of ABP monitoring is well established and many information provided by ABP monitoring as relevant prognostic factors in hypertension have been identified. They include 24-hour average BP, daytime (awake) BP, night-time (asleep) BP, nocturnal dipping of the BP and BP variability.

However, the clinical use of ABP monitoring in individual subjects to optimize their management is not so simple and immediate and measurements should be interpreted carefully.

In the last few years we developed some algorithms for the clinical use of ABP monitoring [4,6-9]. Nevertheless, some recent insights in the interpretation of ABP profile need to be taken into account to help clinicians in the prognostic evaluation of their untreated hypertensive subjects.

## Ambulatory Combined with Office BP

If we plot office BP vis-à-vis the average daytime ABP, it is clear that for any given value of office BP, the observed ABP may vary considerably from the predicted value<sup>10</sup>. Thus, the combined use of office BP with one of the available techniques to estimate out-of-office BP (home or ABP) may identify four different clinical categories of subjects [10]:

- Subjects normotensive by both methods (true normotension);
- Subjects hypertensive by both methods (true hypertension);
- Subjects who are hypertensive based on office BP and normotensive by ABP or self-measured BP (white-coat hypertension, WCH);
- Subjects who are normotensive by clinic BP and hypertensive by ABP or self-measured BP (masked hypertension, MH).

The CV risk in MH seems to be equivalent to that in sustained hypertension. A recent meta-analysis [10] of observational studies

documented that the risk of major CV disease was higher in subjects with MH than in the normotensive subjects regardless of the definition of MH based on self-measured BP (hazard ratio [HR] 2.13; 95% confidence interval [CI]: 1.35-3.35;  $P = 0.001$ ) or 24-h ABP (HR 2.00; 95% CI: 1.54-2.60;  $P < 0.001$ ).

Conversely, the long-term outcome of patients with WCH remains uncertain. In this context, a recent analysis of the PIUMA study [11] showed that the differences in event-free survival between the normotensive group and the group with WCH defined by an average daytime ABP  $< 130/80$  mmHg were not significant ( $p = n.s.$ ). Thus, a daytime ABP  $< 130$  mmHg systolic and 80 mmHg diastolic may be defined optimal to identify WCH with low CV risk, not dissimilar from clinically normotensive participants.

## Daytime Ambulatory BP

Average 24-hour, daytime, and night-time BP values have been the principal components of the ABP profile to be investigated as prognostic determinants.

Although it is generally agreed that the adverse effects of hypertension are related to the average ABP level to which target organs have been exposed over time, reference values are still uncertain because there is paucity of data allowing a shared definition of the values of ambulatory systolic and diastolic BP dividing up normotension from hypertension. Currently, an average daytime BP  $< 135$  mmHg systolic and  $< 85$  mmHg diastolic is generally considered normal, and levels  $< 130/80$  mmHg may be considered optimal [4].

## Dipper Status

The clinical significance of day-night ABP differences has been the subject of an extensive literature. According to whether hypertensive patients have a greater or smaller fall in night-time BP, it has become usual to subdivide them into "dippers" and "non-dippers". Generally, non-dippers are defined by a reduction in BP by less than 10% from day to night, and the subjects out of this definition are classified as dippers [9].

Addressing the issue of the CV risk associated with a less than physiological fall in BP during night sleep, several groups have

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demonstrated the adverse prognostic significance of a blunted day-night rhythm of ABP [12].

### BP Variability

The hypothesis that increased short-term BP variability may contribute to increase CV risk in hypertensive patients is attractive and received an increased deal of attention.

When estimated by the standard deviation (SD), high night-time systolic BP variability identifies hypertensive patients at high CV risk. In this context, a recent analysis of the PIUMA study [13] documented that after adjustment for several confounders, a high night-time systolic BP variability (SD > 10.8) was associated with a 51% excess risk of cardiac events.

### Pulse Pressure

A significant association has been noted in several studies between pulse pressure (PP) and subsequent rate of CV morbid events [14,15]. In order to investigate the prognostic value of ambulatory PP we studied 2,010 initially untreated and uncomplicated subjects with essential hypertension from the PIUMA database [16]. The rates of total CV events (per 100 persons per year) in the 3 tertiles of the distribution of average 24-hour PP were 1.19, 1.81 and 4.92, and those of fatal events

were 0.11, 0.17 and 1.23 (log-rank test: both p <0.01). After controlling for concomitant risk markers, including WCH and the day-night BP change, survival data were better fitted by the model containing ambulatory PP than by that containing office PP. For any given level of office PP, CV morbidity and mortality markedly increased with average 24-hour ambulatory PP.

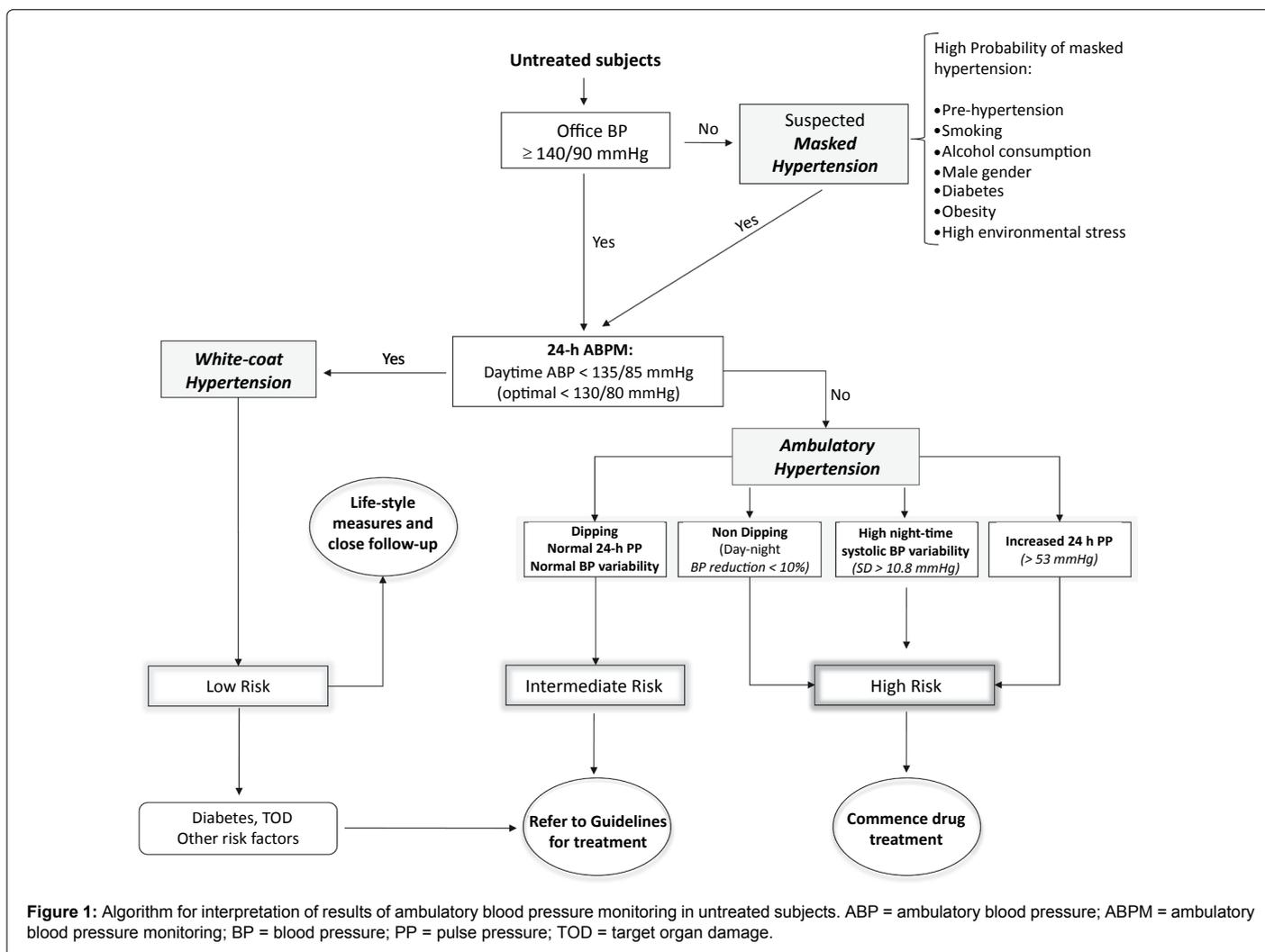
### Practical Approach

For a correct interpretation of ABP profile, we need to evaluate ABP components (systolic, diastolic and PP) comparing them with reference values.

For a complete description of the results during interpretation, we recommend the use of a mnemonic: Ambulatory Does Prediction Valid (ADPV):

- Average ambulatory BP
- Dipping pattern
- Pulse pressure
- Variability of night-time systolic BP

Figure 1 depicts an updated algorithm that could be used to refine CV risk stratification and adapt treatment strategies. Office BP (or



home BP if available) is the first line procedure to identify subjects who could be candidate for commencing drug treatment. In the subjects with normal office BP, 24-hour ABP monitoring identifies low-risk individuals with normal or optimal values of daytime ABP (i.e., WCH). These subjects are suitable for life-style measures without antihypertensive drugs if they are free of comorbidities and target organ damage.

In contrast, a non-dipping BP pattern, an increased 24-hour PP or an increased night-time systolic BP variability in subjects with elevated daytime BP (i.e., ambulatory hypertension) identify high-risk individuals, regardless of office BP values (office hypertension or MH). In these subjects, drug treatment should be started as soon as possible.

Indications from current guidelines remain mandatory in subjects with intermediate risk levels based on ABP, as well as in subjects with WCH and associated risk factors<sup>1</sup>.

#### Disclosure

None of the authors of this study has financial or other reasons that could lead to a conflict of interest.

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