Computer analysis of blood pressure indices

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Blood pressure measurements over 24 h The past decade has seen a development of the concept of hypertension from a straightforward elevation of office blood pressure measurement to a classification based on how that elevation is spread throughout day and night in terms of degree and variability. The indices used for these classifications are derived from ambulatory blood pressure measurements linked to existing and subsequent development of surrogate end-points and the occurences of cardiovascular events in patients.

Presentation of results It is ironic that the raw indices are presented to the physician to aid diagnosis when this information was the basis for their original development. It would be more practical and logical for software to present results of ambulatory blood pressure measurements in a natural language summary and diagnosis rather than reducing the data to simple statistics.

Computer aided-treatment Computers can be used to go further and suggest treatment which, after all, is a consequence of the diagnosis. In this way computers can be used as true analytical partners rather than sophisticated calculators.

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Introduction

Measurement of blood pressure has been performed for the last hundred years [1,2], but such a measurement has little use unless it becomes an index. So what is a blood pressure index? A blood pressure index is an indicator of the level of some aspect of blood pressure, the prolonged abnormality of which contributes to target-organ damage.

Over the years there has been a steady development of blood pressure indices, particularly in more recent times because of the availability of accurate ambulatory recorders [3]. These broadly fall into four distinct classes that are outlined in this review.

Indices of usual blood pressure

The most basic estimate of usual blood pressure is a single office measurement (also referred to as clinic or casual blood pressure). The underlying assumption behind this is that a measurement taken at random is *de facto* a typical one and therefore indicative of a usual one. If the result is normal, the single measurement often stands as the definitive index. If it is abnormal, a set of measurements is usually made. Both arms may be used and measurements can be taken over more than one visit. The mean of these measurements is then usually regarded as the index [4–6].

Some of the elements which can make these measurements anything but typical are measurement errors [7–10], the observer status [11], the sex of the observer, the time spent resting before the measurement [5], the posture of the patient at the time of measurement [12,13] and the anxiety level of the patient [14]. It is precisely because some of these elements tend to raise blood pressure [15] that multiple measurements are made when elevation is noted on a first measurement. Yet the conditions under which the subsequent measurements are made remain largely unchanged.

Ambulatory blood pressure measurement has provided a means of obtaining a more detailed picture of blood pressure. Mean daytime and night-time blood pressures are universally used as summary statistics of ambulatory blood pressure measurements. In many instances a short initial window, such as the first hour [16], is analysed separately as the 'white-coat window'. This is because the same influences that may raise blood pressure during office measurement [15] are generally present at the time of fitting the monitor.

The mean daytime blood pressure is affected by the day's activities. The results are influenced, for instance, by whether or not the recording was made on a working day [17,18], a rest day or a day on which the subject was confined to bed. Within these constraints, the level and type of activity undertaken [19] along with smoking habits and food and alcohol consumed on that day have huge influences on the results [20,21]. The question as to which one of these possibilities is the most usual cannot easily be answered; in a sense they can all be considered as 'usual'.

Where there is evidence of pressor effects in an ambulatory blood pressure measurement, the median pressure may be a better estimate of usual blood pressure as this is less affected by short periods of atypical behaviour such as a period of stress or, on the other hand, a short siesta. While changes in response to these are important in themselves, they do not represent usual blood pressure levels but aspects of variability.

Night-time blood pressure is not subject to as many compromising influences as daytime blood pressure and its importance is becoming increasingly recognised [22–27]. Some concern has been raised regarding sleep disturbance due to the measurement process itself and the consequence this has on blood pressure. However, it seems that, where there is a reaction, it is delayed and that the measurement has already been taken before the patient responds to the disturbance.

The emergence of two fundamental upper limits of normality introduced new concepts of hypertension. There has been a distinct reluctance to bring sex, age and geographical location into the picture because of the multiplicity of norms and consequential confusion that this may bring.

Indices of blood pressure variability

It is not surprising that this class has received most attention since the introduction of 24-h ambulatory blood pressure measurements. Prior to these 24-h ambulatory measurements, blood pressure measurement was simply not practical on a scale that would produce clinically applicable results.

Variability falls into three categories: diurnal variation, nocturnal variation and circadian variation. The standard deviation is most widely used for the first two of these with the coefficient of variation being also used in some cases. However, despite their widespread use, no attempt has been made to turn them into true indices by setting out markers of abnormality. In particular, the interinfluence of activity, food and alcohol consumption with postprandial dips, siesta dips, smoking habits and evening changes [19–21] which, in turn, have underlying geographical [28–30] and seasonal [31–35] influences, on daytime variability compromises a global picture and the ability to extract the true underlying variability. However, examination of changes observed on a population basis may identify problems at an individual level where the influences are missing or exaggerated and also may partly explain regional effects on the risks of target-organ damage.

As in the first class above, nocturnal variation is not influenced by nearly as many factors as daytime blood pressure variation. This is another aspect of nocturnal blood pressure that needs further research.

The main focus on variability has been on circadian variation, in particular the importance of a nocturnal dip [36]. Calculated either empirically (the straight difference), or as a percentage of daytime blood pressure, markers were quickly published. The sheer simplicity of its calculation also ensured its widespread usage. It has, however, also been subject to criticism. This has generally centred on the assumption that blood pressure drops at night from a daytime reference whereas, more correctly, it rises during the day from a night-time baseline. However, previously there had been a long established acceptance of what was normal office blood pressure that, in the absence of any other reference point, was directly translated to define normal daytime blood pressure. There had been no large-scale research on nocturnal blood pressure to provide levels of normality. Proper limits of normality for daytime and night-time blood pressure only came with the large population studies that followed later [37,38].

Other parameters have also been used to measure variability without the need for predefined definitions of daytime and night-time periods. Cumulative sums analysis [39] with the derived statistics, height of cumulative sums, circadian alteration magnitude and square wave analysis [40], have also been used to summarize circadian variation. Fourier [41,42] and spectral [43–46] analysis have also been used with the advantage of including all three sources of variation. Fourier analysis also combines blood pressure level and variation.

Indices of 24-h blood pressure

Twenty-four-hour mean blood pressure has been a popular statistic since the introduction of ambulatory blood pressure measurement. Its expected result, however, is anything but a representative reading. The 24-h mean will be lower than most daytime blood pressures and higher than most night-time blood pressures because of the bimodality of 24-h blood pressure. Only in the case of non-dippers will the value be statistically meaningful. However, this does not detract from its potential as a useful index. If the daytime and night-time means are calculated separately and then combined into a new time-weighted mean, this would have the same value as the original 24-h mean (there would be a reduction in the accompanying standard deviation). As this is the correct manner in which to achieve this result, it should be referred to as the 24-h weighted mean.

Another useful index of 24-h blood pressure is blood pressure load, detailed below, which, regardless of the formula used, is calculated relative to a limit appropriate to the time of day.

Indices of blood pressure excess

In most ambulatory blood pressure measurement patterns, blood pressure exceeds the upper limit of normality on some occasions despite the fact that overall averages may be quite normal. The question arises whether there is a relationship between target-organ damage and blood pressure in excess of the upper limit of normality. This excess is known as 'load', and was first introduced by Zachariah *et al.* [47] as the percentage of measurements above normality. It has the advantage of being easy to calculate but, while still in popular use, takes no account of the levels of pressure involved. White [48] addressed this by defining load as the area under the curve above the upper limit of normality. For moderate or severe hypertensive patients, daytime and night-time load values by this definition are similar to the mean value less the upper limit of normality. However, this similarity ends as the mean level drops toward and into normotensive ranges.

The concept was brought a stage further by Atkins *et al.* [49] who suggested that load should be defined as the area under the curve above the upper limit of normality expressed as a percentage of the area under the curve above the average of normality [49,50]. This took all the advantages of White's definition but added some refinements. First, the range was between 0 and 100, a unitless and easily identifiable range. Second, it is most sensitive in the lower ranges; this is precisely where measurements above normality are swallowed up in the mean. It is less sensitive to changes in the extreme upper range; this corresponds to the fact that changes in the extremes are of less benefit than similar changes in lower ranges, for example a drop of 20 mmHg from 220 mmHg to 200 mmHg is not as beneficial as a drop from 165 mmHg to 145 mmHg. For comparison the corresponding load changes for a theoretical series of constant values are given in Table 1.

This latter definition of load also has a hypotensive compliment, leese, which is defined as the area under the curve below the lower limit of normality expressed as a percentage of the area under the curve below the average of normality.

With office blood pressure there is essentially one index but ambulatory blood pressure measurement has enabled several more to be developed and, no doubt, there are several more to come. These will in turn bring about more classifications of hypertension which will affect patient treatment. This research highlights a two-pronged approach to the analysis of ambulatory blood pressure measurements. On one hand, various nuances in ambulatory blood pressure measurements are being studied to identify the subtle changes indicating the development of hypertension and various types of hypertension. This demonstrates the inherent complexity of ambulatory blood pressure measurements. On the other hand, ambulatory blood pressure measurements are summarized to a few mean values in an attempt to simplify them; in a sense they are being brought back to a single office blood pressure.

Measurement techniques have advanced enormously in most aspects of medicine and, outside of specialist units, it is impossible for physicians to learn every aspect of these new results and to keep up to date with all the research. For this reason, complex results tend to be summarized back into familiar references. This approach seriously compromises the potential of the techniques, however, and severely dampens the impact of research involving indices other than very simple summary values.

So far, computers have essentially been used merely as sophisticated calculators in the production of indices, but the very research that developed the indices involved their relationship with cardiovascular morbidity and, possibly, mortality. Why is it then that physicians are presented with raw data, a set of blood pressure, risk factor and target organ indices? All of the rules for combining these can be programmed into a computer so that the computer can analyse the data and a natural language diagnosis can be produced. A physician could change the diagnosis but should document why so that improvements can be made to the computer's analysis. Of course, once a diagnosis has been made, the treatment programme is usually a matter of following just another set of rules and thus there is no reason why the computer cannot also suggest treatment.

Table 1 Corresponding load changes for a theoretical series of constant values.

Definition of load	Blood pressure (mmHg) 220	200	165	145
Zachariah *et al.* [47]	100	100	100	100
White [48]	80	60	25	5
Atkins *et al.* [49]	84	80	63	25

This is not a picture of some futuristic clinic whereby a patient sits on some technochair, has all functions tested and then automatically receives a diagnosis and prescription. It is rather a more accurate and fairer way of enhancing current procedures.

Because of the difficulties in closely analysing ambulatory blood pressure measurements, software, particularly proprietary software, simplifies this by concentrating on basic summary statistics. Fundamentally this is the diagnosis. The patient is either normotensive or mildly, moderately or severely hypertensive. The physician has a standard treatment for each case. It is all but automatic.

Ultimately the role of the physician is to care for patients. As the amount of data available increases exponentially, it will no longer be possible to manually assess all of it. The option of reducing it back to simple statistics will become less and less tenable. The other option is to welcome the computer as a partner in diagnosis and treatment. Perhaps it is appropriate that this new role for computers coincides with the dawn of the 21st century.

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