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Research Article

# Derivation of a measure of systolic blood pressure mutability: a novel information theory-based metric from ambulatory blood pressure tests

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## Abstract

We provide ambulatory blood pressure (BP) exams with tools based on information theory to quantify fluctuations thus increasing the capture of dynamic test components. Data from 515 ambulatory 24-hour BP exams were considered. Average age was 54 years, 54% were women, and 53% were under BP treatment. The average systolic pressure (SP) was 127 ± 8 mm Hg. A data compressor (wlzip) designed to recognize meaningful information is invoked to measure mutability which is a form of dynamical variability. For patients with the same average SP, different mutability values are obtained which reflects the differences in dynamical variability. In unadjusted linear regression models, mutability had low association with the mean systolic BP ($R^2 = 0.056$; $P < .000001$) but larger association with the SP deviation ($R^2 = 0.761$; $P < .001$). Wlzip allows detecting levels of variability in SP that could be hazardous. This new indicator can be easily added to the 24-hour BP monitors improving information toward diagnosis. J Am Soc Hypertens 2016;10(3):217–223. © 2016 American Society of Hypertension. All rights reserved.

*Keywords:* Blood pressure; cardiovascular risk; hypertension; variability.

## Introduction

Blood pressure (BP) can reach persistently elevated levels in what is usually called hypertension, a condition with one of the highest mortality rates worldwide. As it is well known a proper diagnosis of hypertension can help to save lives and to avoid vascular accidents that can limit the quality of life of some patients even if they survive.[1] The cardiac cycle is very well established and can be found in the classical physiology textbook of W.F. Ganong for example.[2] The systolic pressure (SP) is the maximum arterial pressure while the diastolic pressure (DP) is its minimum pressure, both of which are usually reported in units on mm of Hg. The SI unit for pressure is the Pascal (Pa) which corresponds to 1 $N/m^2$; the kPa is found to be more convenient for usual BPs. The conversion can be easily achieved by means of the following expression: 1 mm Hg = 0.13332 kPa.

We can refer to the two previously mentioned circulatory pressures by an ordinate pair of numbers (SP,DP) for convenience with average values over a certain period of time denoted by (<SP>,<DP>). Thus, daily average pressures like (<125>,<75>) are usually thought to describe a person with normal BP; likewise, (<140>,<85>) describes a patient with some degree of blood hypertension. Although classifications of stages for hypertension may vary among different sources in this article, we follow here the study by H. Prat el al[3] due to its local implications, since we will be dealing with data recorded in Chile.

Single measurements of BP may not have real significance for BP varies during the day. Therefore, a sequence of

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measurements is more appropriate since BP changes in intervals of minutes for the same person. An ambulatory 24-hour BP monitor (BP Holter) has been implemented, that periodically records SP, DP, and heart rate (HR) aiming to improve diagnoses. This monitoring system has been in use in Chile for decades using well-established protocols.[4] The BP Holter examination can be adjusted to provide information after periods of certain number of minutes and during the course of many hours (usually one entire day). In this article, we will use this kind of data as described in the next section.

Usually, the data sequence provided by the BP monitors is subject to basic "static" statistics. In the present study, we propose a way to extract additional information from the ambulatory BP monitor, which can be used by the treating physician to determine "dynamic" variability in the series of measurements. By means of information theory, it is possible to recognize the degree of information content in any sequence as has been successfully applied in the case of magnetic systems.[5] The same technique has been applied to study the dynamic variability of economic systems as well, such as stock markets.[6] This new method introduces a quantitative indicator called mutability ($\mu$) that recognizes the repetitive structures in the data chain. For the time being, let us just say that $\mu$ is a measure of the agitation of the system revealed by the fluctuations of the data sequence; high values of $\mu$ correspond to highly changing variables, while low values of $\mu$ correspond to monotonic data.

Although the importance of static variability in BP has been discussed in relation to prognosis and as a therapeutic target,[7–9] it is not measured in clinical practice due to the lack of universally accepted definitions for normality or risk. We believe mutability may add information in relation to this field because it can deal with variability in a dynamic way which is not done by normal statistical methods. We will present evidence for recognition of different BP patterns by means of mutability, which could be an indication for risk. At present, there is no clinical evidence to sustain a risk indicator, so this represents the introduction of new techniques based on information theory. This should be considered as a first step research in relation to hypertension information and further studies relating these data with clinical outcomes are needed.

## Methodology

### *Data Description*

The data used in the present study correspond to a random selection of 515 BP Holter tests obtained at *Clinica Alemana de Temuco*, between June 11, 2006 and November 10, 2011. Owing to Chilean laws and the regulations at *Clinica Alemana de Temuco* access to patient's personal or clinical information is not available to us; the only additional information that can be used here is some general demographic characteristics like gender, age, and medication or no medication. The Ethics Board of Universidad de la Frontera has approved the protocol for handling the data used in the present study. An arbitrary code number has been assigned to each data sequence as a way to label it, but this contains no information that could lead to the patient identification.

Measurements were done automatically by means of an ambulatory 24-hour BP monitoring system (Mobil-O-Graph), with a cuff of either 600 mm long and 140 mm wide or 550 mm long and 135 mm wide according to the circumference of the arm. It was positioned by a trained nurse on the left arm over the brachial artery. Patients were instructed to extend their left arm on hearing an acoustical signal and to remain quiet while the measurement was under way. After 24 hours, the patient returned to the clinic where the BP monitoring system was removed and the data was downloaded. The monitor was placed on the patient in the late morning hours and withdrawn the next day around the same time, which usually meant the loss of a few registers for some patients just before noon.

From an initial random selection of over 600 examinations, we left only the 515 that were successful in at least a 90% of the daily attempts to measure the three quantities already mentioned in the previous section were as follows: SP, DP, and HR. Measurements were recorded every 15 minutes from 7 AM to 11 PM and every 30 minutes otherwise, which means that the ideal number of daily measurements is 78. Because not all patients presented the same number of successful measurements, a relative statistical treatment is defined in the following paragraphs.

The examination was analyzed and reported by an expert who commented on the data according to general statistics. Particular attention was paid here to the SP since it has been found it is particularly linked to vascular risk.[10] In summary, the following basic statistics could be obtained from this examination: total number of valid measurements, daily average values <SP><DP><HR>, average values for day and night, maximum and minimum registers for these periods of time, dipper or nondipper behavior, and standard deviations. All these results were based on statistics over the final distribution of the records. Our proposal will consider dynamic recognition of the records during the measurement period.

We can group patients according to general characteristics only: sex, age group, and also according to whether they are already under treatment (medicated) for hypertension or not. As already stated, other personal or clinical information was not known to us. This study will emphasize SP records provided by the 24-hour BP monitors.

We have classified the patients in a very general way according to their average SP. After a long discussion in relation to BP threshold values, we have chosen the criteria proposed by NICE, by the JNC7, and the European Societies of Cardiology and Hypertension.[11] This means that we adopt the consensus for normal ambulatory BP